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SYMPOSIUM ON THE SIGNIFICANCE OF BLOOD SUGAR*

INTRODUCTORY REMARKS OF THE CHAIRMAN

H. O. MOSENTHAL
New York

Members of the Section of Medicine, members of the New York Diabetes Association, and guests:

A brief survey of the purpose of this symposium may not be out of order.

Every doctor treating diabetes patients is constantly confronted with the question: What is the ideal blood sugar level? There are some facts in regard to blood sugar about which we are well informed; there are others, however, concerning which we are ignorant.

We know the normal figures for blood sugar and also that in many older persons the blood sugar concentration often exceeds the accepted normal averages; it is also appreciated that in many cases of diabetes under careful insulin treatment the blood sugar fluctuates a great deal and may not be under satisfactory control at certain times of the day, especially in the morning.

What we do not know is how the level of the blood sugar in itself, apart from glycosuria or acidosis, affects human beings. Does a high concentration of sugar in the blood favor bacterial growth and the occurrence of infectious diseases? Is hyperglycemia responsible for the rapid development of vascular changes so often found in diabetes? What effect has an elevated blood sugar upon the nutrition of the tissues such as the heart muscle?

* Presented at a Combined Meeting of the Section of Medicine and the New York Diabetes Association, January 21, 1936.

Clinicians are eagerly awaiting an answer to these problems so that the objectives of treatment in diabetes may be more clearly defined.

There are in this country no scientists or clinicians better qualified than the three essayists of the evening, to inform us upon these questions and it is with genuine pleasure and anticipation that we welcome our guest speakers.

The Effects of Carbohydrates on Bacterial Growth and Development of Infection

Stanhope Bayne-Jones
New Haven

There are two parts to the title of my paper and I shall use the liberty presented by that title to deal with the two parts separately, and then try to bring some of this knowledge together and indicate possible conclusions. I may say at the start that while we know a great deal about the effect of carbohydrates upon bacterial growth in test tubes, we know relatively little about the processes of infection and resistance. There is even less information about the effect of various concentrations of carbohydrates upon the functions of the cells concerned in opposing bacterial growth in tissues. It will be difficult, therefore, to indicate the practical bearings of this incomplete knowledge or to describe the definite relationships of all the parts.

If you will permit me to do so, I will review, for those who are not working in the bacteriological field, some of the things with which the bacteriologist is concerned when he studies the effects of carbohydrates upon the growth of bacteria.

Multiplication of organisms is usually regarded as the evidence of growth. For practical purposes, little misunderstanding will occur if increase in numbers of cells of the normal size is taken as the definition of growth. Nevertheless, this definition may at times be faulty. From a number of years of study of motion pictures and calorimetric observations of bacterial cultures I know that multiplica-

tion by continued subdivision of cells may occur with little or no increase in the bulk of bacterial protoplasm. Hence it is essential to recognize that the true criterion of growth is increase in the mass of bacterial substance.

Growing bacteria have two chief metabolic processes. One is the structural process; the other is the energy exchange. In these respects bacteria are very much like animal cells. They require relatively small amounts of nitrogen for their structural processes, but require a large amount of combustible material, usually carbohydrate, for their energy-needs. When bacteria have the opportunity to get energy from easily combustible carbohydrates, they use sugars in preference to proteins in the medium. The general rule of protein sparing action of carbohydrates applies to bacterial cultures as it does to animal metabolism.

The presence of a fermentable carbohydrate in a medium greatly influences the initial growth, development and fate of a bacterial culture. As is well known, for example, media unfavorable to the pneumococcus will support the growth of this organism if dextrose is present. Avery's medium, used during the war as a substitute for the white mouse, is a typical case. Many others might be cited. Arguing by analogy for these known effects, many persons have supposed that the increased concentration of sugar in the blood and possibly in the tissues in diabetics provided unusually favorable media for bacterial growth and hence aided infection.

I fail to see that this is directly applicable. Most of the media which are rendered more favorable for bacterial growth by the addition of carbohydrate are primarily incapable of supporting more than a feeble development of the organisms. On the other hand, blood and tissues are in themselves such favorable media that the addition of carbohydrate to them can have relatively little effect. That this is so has been shown by a number of experiments, the results of which disclosed that blood to which 0.1 to 0.5 per cent dextrose was added was no more suitable as a culture medium for staphylococci than the control samples without added sugar.

The end products of carbohydrate metabolism, acids, aldehydes and other substances exert unfavorable actions upon bacterial growth, limiting it or suppressing it altogether. None of these actions can come into play in the changing blood stream or tissues of a diabetic.

The effects of fermentable carbohydrates upon the products of bacterial metabolism are particularly noteworthy. Concentrations of dextrose of 1 per cent or more in peptone media may inhibit indole production by colon bacilli, or prevent the elaboration of proteolytic and liquefying enzymes by various organisms. The concentrations of sugar effective in these ways are much greater than those found in the blood of diabetics. If they should exert any influence in the diabetic animal these influences would be protective rather than harmful.

The knowledge accumulated by bacteriologists from the study of the formation of bacterial toxins is especially interesting in connection with infection in diabetes because the concentrations of carbohydrates in favorable media is within the range of the blood-sugar concentrations in diabetes mellitus. Most of the bacteria which produce soluble exotoxins in culture media require 0.1 per cent to 0.3 per cent of fermentable sugar for maximum toxin-production. In preparing modern media for the production of diphtheria toxin 0.15 per cent to 0.3 per cent of dextrose, or dextrose and maltose, are added to the basic proteose-peptone broth. The results obtained appear to indicate that there may be a possible relation between toxin-production in carbohydrate broth and infection in diabetes, and it is possible that this apparent relationship may be a basis for the clinicians' belief that blood-sugar and susceptibility to infection are directly correlated.

In practical bacteriology, however, concentrations of sugar surpassing those found in diabetic blood may be used with similar effects. Additions of carbohydrate until the concentration reaches 0.5 per cent of fermentable sugar will continue to permit the diphtheria bacillus to produce large amounts of toxin.

It is obvious from these facts that the carbohydrate metabolism of certain pathogenic organisms is extremely important for the elaboration of poisonous substances. But the actual connection between this process and infection in diabetes has not been demonstrated.

Bacterial virulence is sometimes associated with the formation of a capsule by the microorganism. As the capsular material is largely carbohydrate, the suggestion has been advanced that abnormal amounts of sugar in the blood may favor the development of a protective capsule by a bacterium in the tissues of a diabetic. Unfortunately for this suggestion there is no support for it to be found in bacteriology. The formation of capsules by bacteria is not strictly correlated with either the amount of fermentable sugar in a medium or the sugar content of the blood of an infected animal. It is, apparently, the expression of an inherent characteristic of a particular race, variety or strain of a species of bacterium.

When we come to the discussion of the second part of my topic, we should recognize at the outset that, although volumes of words may be used to describe conditions, no one can tell absolutely why one animal is resistant to infection and why another is susceptible, or why states of susceptibility and resistance vary from time to time in the same animal. Virulence of bacteria is definable only in terms of the host, and the definition of the resistance of the host must take into consideration some peculiar invasive or toxic effect of the bacterium. Thus the discussion of the development of infections in normal persons and persons suffering from chronic sickness inevitably leads into unsolved mysteries.

The infections of special interest to the physicians treating patients suffering from diabetes mellitus undoubtedly occur most frequently in those who have severe or uncontrolled diabetes. These complications are chiefly staphylococcal infections of the skin, subcutaneous tissues and blood stream. Infections with other organisms are said also to be more numerous and more apt to be severe in diabetics than in persons who do not have this metabolic

disorder. The question why infection is more common in uncontrolled diabetes than in other chronic metabolic disorders and possibly other chronic infectious disease has been a subject of study for a long time. I think that the most illuminating recent discussion of it is the paper by Dr. Mosenthal,[1] published last year. In fact, this paper contains summaries of most of the published scientific information that one may bring to bear on the discussion.

Dr. Mosenthal's final conclusion was that the concentration of dextrose in the blood of a diabetic was not directly related to resistance or susceptibility to infection. He expressed the belief that persistent glycosuria and loss of water over a long period were the factors which diminished the resistance of the patient.

I have asked Dr. Mosenthal what he believes is the mechanism back of glycosuria and dehydration which brings about diminished resistance to infection. It is difficult for me to see how those factors would operate on the cells, skin or other tissues of the diabetic in such a way as to render them more susceptible to bacterial invasion. I hope that later this evening Dr. Mosenthal will have more to say on the ultimate processes involved in this theory.

In my opinion the investigators who are working on the histology of the lesions and tissue changes in diabetes on the one hand and the endocrinologists on the other, have the possibility of explaining not only the incidence and course of infections in diabetes, but also the fundamental physiology of immunity, resistance and susceptibility. As you know, Dr. Reimann[2] found by experiment that patients with uncontrolled diabetes did not produce agglutinins in as high potency as controlled diabetics or normal persons. From this he suggested that in uncontrolled diabetics the capacity to produce antibodies against bacteria was reduced. Recalling his observations that in kala azar the

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1 Mosenthal, H. O. Hyperglycemia. *Jour. Am. Med. Assoc.*, 1935, *105*, 484.

2 Reimann, H. A. Immune Reactions in Diabetes. *Arch. Int. Med.*, 1935, *51*, 789.

endothelial cells of the skin and other organs contain great numbers of parasites, Dr. Reimann has suggested further that perhaps in severe diabetes the endothelial system may be adversely affected. From pathological investigations it has been known for a long time that endothelial cells in certain diabetics are actually crowded, perhaps blocked, with foreign material, fat or other substances. Although these relationships required by this theory have not been definitely demonstrated to exist, the evidence for them is suggestive and interesting.

As a precautionary note it should be remarked that there is no absolute correlation between agglutinin titre in the blood serum and the degree of resistance or susceptibility to infection. I have seen septicemia in a patient whose blood serum, diluted 1-100,000, agglutinated the bacterium cultivated from his blood. The organism did not appear to be agglutinated in the patient's blood vessels. Hence, it is not possible to draw from the results of agglutination tests conclusions applying to the state of resistance of an animal.

In recent days more and more attention is being paid to the relation of the glands of internal secretion to states of resistance and susceptibility. Notably in diabetes the pituitary, pancreas and adrenal are known to have important connected influences. From both published and unpublished observations it appears that these endocrine glands, particularly the pancreas and adrenal, may control some of the processes of defense against invading bacteria. The immunologists are beginning to enter this field. For years, however, physiologists studying experimental diabetes and the inter-relation of glands of internal secretion have been passing over events of great importance to the immunologist and clinician. The physiologists have given little more than cursory notice to the occurrence, characteristics and course of infections in the animals from whom they have removed one or several glands of internal secretion and whose diabetes or other metabolic disorder they have regulated by the administration of extracts of these glands. For example, I know that Dr. C. N. H. Long

and Dr. Himwich have considerable information on immunological problems in their physiological notebooks. We hope very much that they will publish accounts of what they have observed.

In view of numerous uncertainties and with the realization that a bacteriologist can not speak with any authority on intricate clinical and physiological questions, I must state my conclusions in somewhat negative terms. In my opinion, (1) the concentration of sugar in the blood of diabetics has little or nothing to do with their states of resistance or susceptibility to infection; (2) such factors as loss of water may operate through effects on some mechanism not yet disclosed; and (3) the causes of these changes in resistance may be found in the interlocked influences of organs of internal secretion affecting not only sugar metabolism, but also the unknown means by which the body cells resist bacterial invasion and the deleterious effects of bacterial products.

Blood Sugar in Experimental Diabetes*

Harold E. Himwich
Albany

I greatly appreciate the honor of being invited by Dr. Mosenthal to participate in the exchange of ideas on the subject of blood sugar in diabetes. Dr. Bayne-Jones has clarified the relationship of blood sugar to infections. My topic is blood sugar in experimental diabetes. There are two points of view in the treatment of diabetes. The first one calls for the maintenance of a normal blood sugar with values between 100 and 140 mgm. per cent. The second point of view permits and even entertains a preference for higher levels of blood sugar as long as they are not accompanied by marked glycosuria and by ketosis. Tonight I shall review the evidence obtained from experimental studies of diabetes and also present new data in order to evaluate these two opposing conceptions of the management of diabetes.

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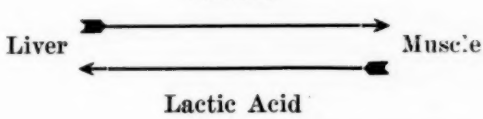
* From the Department of Physiology and Pharmacology, Albany Medical College, Albany, N. Y.

It is interesting to recall that the liver is the source of the blood sugar. After ingestion of carbohydrates, blood sugar rises, a result of the exogenous carbohydrates, but in the post-absorptive state, the level of the blood sugar is

FIGURE I.



maintained by the breakdown of liver glycogen. With Doctors Chambers, Koskoff and Nahum,[5] we were able to show that in diabetes, as in normal conditions, the mechanism which maintains blood sugar links muscle and liver in an intimate manner. Glycogen is not retained by the liver but breaks down to glucose, giving rise to the characteristic hyperglycemia of diabetes. This glucose circulates in the blood, is absorbed by all the organs, and particularly so by the large masses of muscle tissue. In muscle, glucose is synthesized to glycogen. However, this glycogen is not locked in the muscles. With muscular activity, it gives rise to lactic acid, and it should be noted, not to glucose. Apparently the ability of muscle to form lactic acid may be impaired but does not cease with the development of the diabetic state. Lactic acid then diffuses out of muscle to blood. This permits the liver to absorb lactic acid from the blood and resynthesize it to form glycogen. In this manner, the hyperglycemic level of the blood is maintained in the post-digestive state during diabetes.

We must examine next the factors which regulate the level of the blood sugar. In this regard the endocrine glands are determining influences. Though inability to oxidize glucose necessarily causes an increase of blood sugar, it should be remembered that the concentration of the glucose of the blood is responsive not only to the secretions of the islands of Langerhans but also to those of other endocrine glands. The anterior pituitary, the adrenal, and the thyroid glands may act either synergistically or sepa-

rately to raise blood sugar. This they do by mobilizing liver glycogen and not necessarily by inhibiting the oxidation of glucose. Acromegaly in 40 per cent of all cases, may be accompanied intermittently by signs of diabetes including an increased blood sugar and a ketosis.[8] The secretions of the anterior pituitary gland influence both carbohydrate and fat metabolism by liberating liver glycogen and stimulating fat oxidation. It is, therefore, incorrect to regard a high blood sugar and a ketosis as due necessarily to exhaustion of the islands of Langerhans. In patients with acromegaly the administration of insulin may be singularly ineffective. This action is explained by Houssay and Biasotti's[8] conclusion that the anterior pituitary gland contains a hormone which inhibits the oxidation of carbohydrate. However, it should be noted that Chambers, Sweet and Chandler[3] believe that the anterior pituitary does not inhibit the oxidation of carbohydrate.

The hormone of the medulla of the adrenal gland, like that of the anterior pituitary gland, affects liver glycogen. Cope and Marks[4] have demonstrated that the secretions of the anterior pituitary and adrenal medulla act synergistically to deplete the liver of its glycogen. In a like manner, overactivity of the thyroid gland tends to diminish liver glycogen and therefore raise blood sugar without, however, inhibiting the oxidation of carbohydrate. Thus the concentration of glucose in the blood is not necessarily a gauge of the function of the islands of Langerhans but is a resultant of the interactions of various endocrine glands. The level of the blood sugar cannot, therefore, be regarded as the sole criterion for the body to oxidize carbohydrate and thus should not be used exclusively as an index for the amount of insulin necessary for the control of diabetes.

Later we hope to show that in contrast with blood sugar, urinary glucose may be of greater significance in determining the dosage of insulin. But first we must consider the effects of a heightened level of sugar in the blood on the metabolism of carbohydrate.

An increased concentration of blood sugar serves as a stimulus to carbohydrate metabolism. In response to the

rise of blood sugar following the ingestion of carbohydrate, glycogen is stored in liver and muscle while the oxidation of glucose is accelerated. In partial diabetes where the carbohydrate mechanisms of the body are impaired but still function to some degree, it is probable that a high level of blood sugar acts as it does in the normal individual to increase the metabolism of carbohydrate. Indeed, even in the diabetes following total pancreatectomy a high level of blood sugar aids in the storage of carbohydrate. Major and Mann[10] found that intravenous injection of glucose increased the deposition of glycogen in liver and muscle of depancreatized dogs. On the other hand, removal of the liver is followed by a gradual and continuous decline of blood sugar. Mann and Magath[11] first studied dogs with pancreas intact and therefore unimpaired ability to oxidize carbohydrate. After hepatectomy, hypoglycemia always developed in these animals. With the removal of the liver, the cycle between muscle and liver was interrupted and the blood sugar decreased. When the glucose of the blood fell to the low level of 20 mgm. per cent hypoglycemic convulsions occurred. These convulsions are, therefore, the response of the body to lack of carbohydrate. Mann and Magath[11] also removed the liver of dogs that had been depancreatized three or four days previously. These dogs initially had the high blood sugar characteristic of diabetes. Following hepatectomy of the depancreatized dogs, glucose was utilized for there was a progressive decrease of blood sugar just as in the non-diabetic animals. However, in the depancreatized animals convulsions, indistinguishable from hypoglycemic paroxysms, occurred at levels of blood sugar higher than 100 mgm. per cent or even 200 mgm. per cent. Thus in diabetes, a decline of blood sugar, even though to values still well above normal, is followed nevertheless by symptoms similar to those of hypoglycemia in the animal with pancreas intact. These data have been interpreted by Lesser[9] to indicate that a concentration of blood sugar greater than normal is necessary for the utilization of carbohydrate during diabetes. With impairment of carbohydrate oxidation, an increased

concentration of blood sugar is therefore compensatory, insuring a better utilization of carbohydrate. The improvement in the metabolism of carbohydrate must have an immediate effect on the utilization of fat, for an increased oxidation of glucose necessarily causes a better combustion of fat. The conception that high blood sugar aids the utilization of carbohydrate is, therefore, of utmost importance in the management of diabetes. It indicates the advantage of maintaining high levels of blood sugar. This applies especially to patients with raised renal thresholds for glucose.

Though a high blood sugar is beneficial, the ingestion of carbohydrate in quantities in excess of the oxidative capacities of the body has an adverse effect. Before insulin was discovered, it was a common experience to observe failure of the insular mechanisms as a result of the ingestion of carbohydrate in quantities greater than could be metabolized by the patient. The overtaxed oxidations became completely, if temporarily, exhausted. Today, however, such consequences are no longer to be feared for the administration of adequate amounts of insulin spares the endogenous mechanisms from an excessive load. Moreover, a higher blood sugar level is not necessarily a strain on the ability to oxidize carbohydrate. Mosenthal[12] has stressed that a high blood sugar may be maintained for long periods with no deleterious effects in patients with diabetes. Indeed, many people with no apparent defect in the oxidation of carbohydrate exhibit levels of blood sugar well above the usual average values. This is in accord with our previous conclusion that a high level of blood sugar is not necessarily a sign of impairment of the functions of the islands of Langerhans but may indicate instead a mobilization of liver glycogen due to overactivity of other endocrine glands.

If an increased blood sugar does not necessarily injure, and may, in fact, aid the metabolism of carbohydrate, where then, does the chief disadvantage of high blood sugar lie? At present, the evidence indicates that a most serious danger in diabetes is dehydration, which may lead to collapse. Dehydration, moreover, is an element of diabetic

coma. The inception of dehydration lies in the production of the ketone acids. With the impairment of carbohydrate metabolism, additional fat must be oxidized if life is to be maintained. However, the diminished ability to oxidize carbohydrate makes the complete combustion of fat impossible. As a result, acetone substances accumulate. Therefore, a specific acidosis, a ketosis, supervenes. This is the characteristic acidosis or ketosis of diabetes. One of the chief compensatory mechanisms to overcome this ketosis resides in the function of the kidney to produce ammonia for the formation of ammonia salts. These ammonia salts of the acetone substances are eliminated in the urine, and in this manner the ketosis is diminished. However, in severe diabetes, ketone acids accumulate more rapidly than the kidney can form ammonia. All the ketone substances cannot, therefore, be eliminated as ammonia salts. For this reason, the sodium of the blood must be utilized for this process. Thus sodium salts of the ketone acids are also excreted and appear in the urine. When sodium leaves the body, it has an entirely different effect than has ammonia, for sodium is a constituent of the body fluids. The loss of sodium would render the body fluids hypotonic, that is, too dilute, if water were not excreted with the sodium. As a result of the diminished sodium content of the blood, water is eliminated and the dangerous dehydration of diabetes supervenes. This conception, presented by Peters[13] describes one of the two mechanisms of dehydration in diabetes.

TABLE I.

A MECHANISM OF DIABETIC DEHYDRATION

1. Ketonuria
2. Sodium Salts
3. Water

As you will note in the table, the first step in the process of dehydration consists of the elimination of ketone substances. The second involves the excretion of sodium as an aid in the elimination of the acetone substances, and finally the loss of water follows that of the sodium salts.

In 1933 Atchley, Loeb, and their co-workers[2] suggested a second potent mechanism in the causation of diabetic dehydration. These investigators studied two patients with severe diabetes. One required approximately 85 units of insulin daily, and the other about 75 units of insulin to maintain the urine free of sugar. In both these patients, insulin injections were stopped for short experimental periods. With both patients a glycosuria, a polyuria, and a dehydration ensued. Despite the fact that in both patients organic acids of the urine increased and in one of these cases the ketonuria was marked, Atchley, Loeb, and their co-workers[2] were able to dissociate the dehydration secondary to glycosuria from that produced by the acidosis and therefore came to the conclusion that glycosuria, of itself, may be a cause of dehydration. That glycosuria can produce dehydration has been demonstrated in previous work of our laboratory. In a paper presented from this platform during the Graduate Fortnight in 1933, [6, 7] we were able to show that concomitant with the loss of glucose in the urine, dehydration occurred. Acute depletion of the body fluids resulted in the development of fever; diabetic hyperpyrexia. In studies now being made in our laboratory at Albany, we are attempting to examine the mechanism of dehydration when there is no ketosis to initiate the loss of the body fluids. We are employing the partially depancreatized preparation used so effectively by Frederick M. Allen.[1] Our animals weigh from 7 to 15 kilos and usually all but one or two grams of their pancreas are removed aseptically. In many respects this preparation resembles that of a human being with diabetes, for not only are some of the external secretions, the digestive enzymes, of the pancreas retained but also a portion of the internal secretions and therefore partial ability to oxidize carbohydrate. Examinations of the blood sugar disclosed, moreover, that the oral administration of one gram of glucose per kilo of body weight produced the typical heightened and prolonged glucose tolerance curve of severe diabetes. Our preliminary observations revealed a close correlation between the amount of glucose excreted in the urine and the total bases, especially

the sodium, of the urine. When sugar was excreted, water was also eliminated and with the water, salts, chiefly, sodium chloride. We next stabilized our animals much in the same fashion as patients with diabetes. They were given carbohydrate, fat and protein in amounts sufficient to maintain caloric equilibrium and insulin in doses adequate to prevent glycosuria. Salt was added to the diet in an attempt to prevent rapid depletion of the sodium reserves. Due to the diabetic condition of these animals, the post-absorptive level of the blood sugar was high, up to 300 mgm. and more. Nevertheless, with the aid of insulin, daily loss of sugar in the urine was not significant. Despite a high level of blood sugar with no glycosuria, there was no polyuria, and no dehydration. High blood sugar of itself produces no dehydration.

This fact is particularly important in human diabetes and especially so in cases of some duration in which the renal threshold rises as the disease continues. These observations leave no doubt that a high blood sugar in patients with diabetes will produce no dehydration when unattended by glycosuria. The next step was to study the effect of glycosuria. To do this we increased the glucose content of the food of these animals. No other change was made in the diet and the dosage of insulin was kept unaltered. Thus, unlike the previous experiments of Atchley, Loeb, and their co-workers, the present observations involved no decreased oxidation of carbohydrate and therefore no accumulation of acid substances. Thus, the only direct effect of this change in the diet was the production of glycosuria. Nevertheless, the glycosuria was accompanied by a polyuria. Though the kidney may concentrate glucose to 10 per cent or more, additional water must also be excreted by the kidney. The glycosuria forces an increased renal excretion of fluids.

In the table are presented the data of one of our animals. They represent the results of three control days just before the ingestion of increased amount of glucose and the analyses of the last three days of an eight day period of glycosuria without ketonuria. The augmented ingestion of

glucose produces a glycosuria. Associated with an increase of glucose is that of the volume of the urine. The polyuria increases the quantities of base or salts of the urine. Apparently water is eliminated with salt. Therefore, there is a direct relationship between the glucose, the urinary volume and the salts excreted. They all increase together. As you can see in the last column the intake of water is augmented. This also must be attributed to the glycosuria. The water supplied to our animals was unlimited. The salt content of the diet was, however, kept constant. With increasing urinary volume, the output of salt or base finally exceeded the intake. As a result, the sodium of the body was depleted. With the loss of sodium and water, dehydration developed. The depletion of body fluids over the period of eight days is evidenced by the loss of weight.

TABLE II.

EFFECT OF GLYCOSURIA WITHOUT KETONURIA ON URINE

Date Jan.	*Glucose Grams*	*Volume CC.*	*Base M.E.*	*Water Intake CC.*
5	0	156	21.0	565
6	0	210	38.6	330
7	0	129	23.7	360
13	44.7	630	65.7	1000
14	77.5	1360	73.0	1400
15	73.2	1200	60.3	1560

TABLE III.

EFFECT OF GLYCOSURIA

Eight Days

		Blood	
	Weight Kilos	*Serum Protein Per Cent*	*Oxygen Capacity Vol. Per Cent*
Control	7.20	6.38	17.60
Dehydration	7.00	7.07	18.94

This decrease of weight correlates with the greater volume of the urine. The diminution of the fluids of the body may also be seen by the increased serum protein and the raised oxygen capacity of the blood, results of dehydration.

TABLE IV.

MECHANISMS OF DIABETIC DEHYDRATION

1. Ketonuria	1. Glycosuria
2. Sodium Salts	2. Water
3. Water	3. Sodium Salts

Here then is a second mechanism of dehydration. As presented in the table, it is initiated by the glycosuria which increases the excretion of water, thus producing a polyuria and finally a loss of salt. In contrast to the mechanism previously described in which the inception of the dehydration was caused by a ketonuria, the loss of sodium preceding that of water, in the present experiments by avoiding ketonuria, it has been possible to demonstrate that the loss of water may be the cause of the depreciation of the sodium reserves of the body.

If this is so, then the administration of added amounts of salt in the diet should prevent dehydration. We gave our animals, depleted of salt and water, an additional 10 grams of salt daily for two days, and despite the continued glycosuria observed in these dehydrated animals, a subsequent dilution of the blood and a gain of weight due to restoration of the body fluids. Water was retained and the salt deficit was made up. Even though dehydration is conditioned by loss of salt, it must be remembered that the cause of the depreciation of the salt of the body is the presence of excessive amounts of sugar in the urine. These observations suggest, therefore, that in the management of diabetes, the examination of urinary sugar is more significant than that of blood sugar. As long as the glycosuria is not excessive, there is no fear of dehydration. A slight glycosuria is, however, only of secondary importance. The loss of a relatively small amount of energy containing substances in the urine is not serious.

The review of the literature and the new evidence leads to the following four conclusions. (1) The level of the blood sugar is a resultant of the activity of various endocrine glands. It is, therefore, not necessarily an index of impaired ability of the islands of Langerhans but may indicate instead hyperfunction of the adrenal, the thyroid, and particularly of the anterior pituitary glands. (2) During diabetes as in the normal, an increased concentration of blood sugar serves as a stimulus to carbohydrate metabolism and therefore is not to be combatted unless accompanied by a definite glycosuria. (3) Dehydration may be a result of glycosuria. The development of a marked glycosuria should, therefore, never be permitted to continue even for short periods. (4) And finally, as a result of the three previous conclusions, it follows that the glucose content of the urine rather than that of the blood should be taken as the criterion of the amount of insulin indicated in diabetes mellitus.

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Blood Sugar in Diabetes Mellitus*

Edward Tolstoi
New York

The blood sugar is an excellent and useful criterion of the behavior of carbohydrate metabolism. Regulated by normal physiological processes, the sugar of the blood has a constancy within definite limits, and in its behavior like other biological constants it tends to return to its original level when the factor for its alteration is corrected. After the complex carbohydrates are simplified by the digestive enzymes in the gastro-intestinal tract, they are carried as glucose by the portal vein to the liver where a molecular rearrangement takes place and glycogen is formed. This biochemical process is not always in one direction. It is reversible, and it is inferred that the liver can also supply the blood with glucose from the glycogen it has stored. It is obvious, therefore, that the liver plays a most significant role in the metabolism of carbohydrates. It is the carbohydrate storehouse, storing the sugars in the form of glycogen and making excellent use of its savings when the organism is in want of sugars and cannot for various reasons

* From the New York Hospital and the Department of Medicine, Cornell University Medical College.

obtain them exogenously. Thus, during a meal rich in carbohydrates, the blood sugar will rise, but a considerable proportion of the excess will be withdrawn by the liver, converted to glycogen and stored, only to be reconverted into glucose and thrown into the blood stream if the blood sugar should fall below the physiological level. By this means the blood sugar in health is kept within definite limits. These are 80 to 100 mgm. per cent during a fasting state. After an average meal the blood sugar may rise to 140 mg. per cent while after a concentrated carbohydrate meal the value may rise as high as 170 or 180 mg. per cent. It must be pointed out, that the role of the liver in this regulating process is more or less a passive one, as there are many factors which affect its activity directly or indirectly. Of such factors intimately concerned with carbohydrate metabolism, insulin plays a most dominant role and all of us are well familiar with the clinical picture which results from the lack of production or faulty utilization of this hormone. This profound alteration in the carbohydrate metabolism primarily, is known as diabetes mellitus and in addition to its clinical symptomatology of hunger, loss of weight, thirst, frequency of urination, weakness, transient blurring of vision and distressing pruritus chiefly in women, there is a hyperglycemia and a glycosuria. The liver is no longer capable of maintaining the blood sugar at the physiological level because one of the governing mechanisms, insulin, is insufficient. There is faulty storage of glycogen and faulty oxidation of glucose. The blood sugar begins to rise and when it reaches a level of 170 or 180 mg. per cent sugar will appear in the urine. This is true in the majority of the cases, though I have seen some blood sugars between 200 and 300 mg. per cent without a glycosuria. The rise of the blood sugar does not cease at the levels mentioned, but it may rise to a figure of 1000 mg. and over.

With this brief resumé of normal and abnormal carbohydrate physiology and with the knowledge that insulin can alter some of the abnormalities discussed, we can now proceed to the discussion of the blood sugar in diabetes

mellitus. Some phases of the subject are controversial and some are quite factual. *The most accepted fact is that the blood sugar in diabetes mellitus is elevated and maintained at a highly abnormal level unless treated.* All agree that the sugar in the blood is glucose—and that it is fermentable. Most physiologists do not accept the γ-glucose hypothesis of Winter and Smith. While there is no unanimity of opinion regarding the glycolytic power of diabetic blood as compared with the normal, the preponderance of evidence is that no difference exists.

About ten years ago I interested myself in the subject of glycolysis sharing the view that insulin acted by increasing the glycolytic rate. This was not the case, however, as I proved to my satisfaction that the sugar content of diabetic and normal blood kept at room or incubator temperature disappeared at the same rate. Glycolysis did *not* proceed at a less rapid rate in diabetic bloods. There is no difference of opinion concerning the effect of infections on the blood sugar in diabetes mellitus. All agree that during infections, it is always elevated. All agree that a normal blood sugar is highly desirable in the treatment of diabetes but not many appreciate the fact that under certain conditions a hyperglycemia per se is not deleterious, but may even be desirable. In other words a high blood sugar *without a glycosuria* can be tolerated by patients without any damaging results.

Specifically, the discussion of the blood sugar in diabetes mellitus may be approached from three practical considerations, namely the value of blood sugar analyses from the point of *diagnosis, prognosis,* and *treatment.* From a study of a large group of glycosurias and a correlation of the blood sugar findings with them I am firmly convinced that from a *diagnostic* consideration, blood sugar studies are of the greatest and most valuable aid. The benign glycosurias are too well known to all of us and in such cases a definite diagnosis can only be made by means of blood analyses. It is the usual procedure in cases of glycosuria to examine the blood for its glucose content in a post-absorptive state and if the result of such an analysis prove inconclusive then

the patient is subjected to any of the well known tolerance tests. The one most widely in use is the so-called glucose tolerance test. The patient is given 50 to 100 gms. of glucose and the blood is examined for its sugar concentration at a fasting, ½, 1, 2 and 3 hour interval. In the normal individual the maximum rise may reach 180 mg. per 100 c.c. At the end of an hour the concentration of blood glucose begins to fall so that at the end of the third hour there may be less glucose in the blood stream than at its beginning of the test. In the diabetic, on the other hand, the fasting blood sugar is usually above the normal level and even if it is reduced to a normal figure by means of diet, insulin or both, a glucose tolerance test, may send the blood sugar up to 300 and 400 mg. even at the end of the third hour.

There are certain cases where the blood sugar may reach a level of 200 at the end of the first hour and a glycosuria may appear at this point, but the curve falls sharply and conforms to the configuration accepted as normal. I do not consider such curves pathognomonic of diabetes. Now all of this is quite familiar, and yet there is an important consideration which must be weighed in the evaluation of any carbohydrate tolerance test, namely the patient's previous diet.

Some years ago a group of Scandinavian[1] observers called attention to the fact that even in normal individuals a 24 hour fast, or a high-fat-low carbohydrate diet will so alter the character of a tolerance blood sugar curve that a false diagnosis of diabetes will be made. I[2] have had the opportunity of performing such an experiment on two men whose diet consisted of protein and fat—an exclusive meat diet. In both subjects typical diabetic curves were produced following the ingestion of 100 grams of glucose. In one of the men there was a glycosuria as well. The use of a general diet for a two week period cured this artificial diabetes as the repetition of the glucose tolerance test at the end of that time failed to reveal any abnormality. It is obvious therefore that the blood sugar is of considerable diagnostic aid in cases of glycosuria, either as a single fasting specimen

or as a series of specimens after a tolerance test. In the vast majority of cases it will help establish, or rule out the diagnosis of diabetes mellitus. I also wish to lay particular emphasis on the consideration of the patient's diet prior to the performance of a tolerance test since it plays such a significant role in the proper evaluation of the resulting blood sugar curve. Diseases of the liver may also be responsible for abnormal glucose tolerance curves and before accepting a curve as significant of diabetes one must make certain that no liver pathology is present.[13]

Is the blood sugar of any prognostic significance? Does the routine estimation of the blood sugar in diabetes mellitus help in the evaluation of the severity of a case? I do not think it does. Some ten years ago Petren[3] attempted to use the blood sugar as a measure of severity and he considered an initial value of 240 mg. or over as an indication of a severe diabetes. Gray[4] pursuing this trend of thought attempted to show the relation of the percentage of the blood sugar when the patient was first seen, to the duration of such a patient's life. From his studies Gray concluded that the higher the blood sugar, the more severe the diabetes. This point of view has been rather universally accepted, but it certainly can stand revision. It requires time and observation of any given case of diabetes before a prognosis can be given intelligently. It certainly is most fallacious to prognosticate from a blood sugar examination alone. I do not consider an initial blood sugar of 300 mg. of more ominous prognostic significance than one of 200 or 150. The deduction that I draw from such figures in the absence of any infection is that the higher blood sugar may be a reflection of the patient's carelessness in executing dietary directions. Joslin,[5] from whose clinic Gray published the data referred to, now feels that the prognosis in a diabetic case can not be determined by the result of the blood sugar test. He cites a diabetic patient who on admission showed a blood sugar of 400 mg. and a glycosuria of 4.8 per cent whose health 20 months later was excellent and whose diet consisted of protein 75, fat 100, carbohydrate 250 and only 6 units of insulin. "One can not tell

from an initial blood sugar," says Joslin, "the outcome of a case though this was not the rule before the discovery of insulin." This fact was fully appreciated by Petren and his coworkers, and, because of this inadequacy of a single blood sugar determination as a prognostic guide, they have attempted to evaluate the severity of the diabetes from a study of the 24 hour blood sugar curve. Blood samples were taken at two hourly intervals during a 24 hour period and the character of the curve served as an index of severity. They have worked out such blood sugar curves for fast days and food days. They also demonstrated that the blood sugar in certain cases of diabetes is subject to tremendous oscillations during a 24 hour period. All these data are of considerable interest, but I question their applicability, as it is not practical to carry out 24 hour blood sugar analyses in most cases, even though this procedure might afford a trustworthy indication of severity. It is my feeling that response to therapy is a much more reliable index of severity, and no single blood sugar determination regardless of its magnitude will dampen my optimism if the patient's glycosuria diminishes, if he gains in weight and strength and if he is able to tolerate more carbohydrates and total calories without any, or additional units insulin.

Now as to the value of blood sugar studies in the *treatment* of diabetes mellitus. I am in accord with the school of diabetologists who advocate a normoglycemia. A normal blood sugar in a diabetic is usually accompanied by a sugar free urine. That is the optimum goal. Given, however, a sugar free urine, but with a blood sugar level of 200 or 250, is it advisable in such cases to aim at lowering these blood sugars even though no sugar is excreted? I do not think so. There is no clear evidence that a hyperglycemia without a glycosuria is damaging, and, furthermore, such a condition may even be desirable in a certain group of diabetic patients. This view may sound unorthodox but a review of the available evidence will help dissipate doubts concerning this assertion.

In the August number of the Journal of the American Medical Association, Mosenthal[6] in a publication entitled "Hyperglycemia," presents evidence bearing upon this question. Therein, he cites the works of Kirby, Estey and Weiner and that of Carrel showing that culture media containing three to four times the normal concentration of glucose do not inhibit or interfere with growth of tissues. He also presents the work of other investigators who claim that bacteria do not grow more rapidly in culture media of high sugar concentrations. Furthermore, he cites the fact that addition of dextrose to blood does not alter its bactericidal potency against staphylococci, nor make growth of this organism more luxurious.

The above data certainly offer striking evidence that under certain experimental states a hyperglycemia in vitro is not deleterious. Then there are other experimental conditions demonstrating the benefits of a hyperglycemia. Bayliss, Müller and Starling[7] showed that in order to maintain heart-lung preparations in good condition insulin and glucose had to be used and that in the absence of insulin, *enormous concentrations of glucose were required* to compensate for the insulin lack. Cruikshank and Shrivastava[8] showed that the sugar utilization of the heart is increased, by insulin, or *by maintaining a high blood sugar concentration.* In other words a hyperglycemia may act as a compensatory mechanism. Clinical observation has given ample support to these experiments. During the past 4 or 5 years observers from various parts of the country have noted that in some cases of diabetes mellitus lowering of the blood sugar, not necessarily to hypoglycemic levels, was associated with symptoms referable to the heart. Levine[9] of Boston issues unequivocal warning against the rapid reduction of a hyperglycemia in a diabetic with coronary artery disease. I have seen one death associated with the use of insulin in a diabetic, who was also suffering from coronary sclerosis. Even though there was a temporal relationship I was not convinced that it was cause and effect as cases of coronary sclerosis may also die without any apparent cause. However, the work of Strouse[10] and his associates on this

subject, made me feel that some such relationship exists. They found that in the older diabetic a marked reduction of the blood sugar whether by insulin or diet was associated with manifestations of cardiac abnormalities such as paroxysmal auricular fibrillation, intraventricular block and the clinical picture of angina. Sherrill[11] of California advises that the hyperglycemia of the elderly diabetic, particularly when evidences of atherosclerotic changes are demonstrable, be handled most conservatively. We thus see from the data presented that hyperglycemia does not interfere with or inhibit tissue growth, that hyperglycemia does not furnish some bacteria—staphylococci—a more fertile soil for growth, and that hyperglycemia may be of benefit in the elderly diabetic patient, who reveals evidence of vascular disease. I have seen a considerable group of diabetics in their fifth and sixth decades whose blood sugars were twice the normal, but whose urines were free from sugar. These patients maintained their weight, they were symptom free and carried on with their daily routine. But as soon as continuous glycosuria set in because of dietary indiscretions or infections then, and only then did symptoms of diabetes become apparent. In certain cases of diabetes mellitus a hyperglycemia without a glycosuria is seen and in such cases it is my feeling that a *sugar free urine is a satisfactory criterion of good therapy* from the laboratory view point. With younger diabetics under such circumstances the blood sugar will in the majority of cases approach the normal figure; in the older diabetic let the blood sugar seek its own level, even though it is above the figure considered normal.

This point of view will no doubt bring forth the criticisms that good therapy must not only ameliorate suffering, it must also prevent complications and a high blood sugar even without a glycosuria may lead to undesirable sequelae, which according to popular medical opinion of many years, are—infections as immediate complications and atherosclerosis as remote. I am not referring to the diabetic who is spilling sugar, I have in mind the patient who has only the hyperglycemia. Is this type of patient more subject to

infections and atherosclerosis than the diabetic with a normoglycemia? From my observations and experience he is not. True I have seen nail infection, boils, tuberculosis, pneumonia, otitis media, mastoiditis and common colds in our group of diabetics, but I do not think that such infections were more prevalent among these patients, than any group of individuals under similar living conditions, and many of our patients revealed hyperglycemic states—some with and some without glycosurias. It is my feeling that this association of infections and diabetes has become so deeply rooted, with the resulting view point that hyperglycemia renders the patient more susceptible to infectious processes. Mosenthal is of the opinion that the tissue dessication and the debility resulting from a persistent glycosuria predipose the patient to infections and that the hyperglycemia per se is not deleterious. Infections, however, no matter how slight, affect adversely the carbohydrate tolerance and are therefore dreaded as complications. Now as to the complication of atherosclerosis. Does a high blood sugar alone favor or hasten the development of vascular sclerosis? No one really knows. The hypotheses are multiple, conflicting and confusing. The experimental evidence of MacLeod[12] failed to corroborate this postulate. He maintained two depancreatized dogs in a state of hyperglycemia and glycosuria for 4 years and was unable to demonstrate any arterial sclerosis. The more fashionable thought is to associate a hypercholesterolemia and ketonemia with atherosclerosis, and furthermore there are many who feel that in an individual with vascular sclerosis and diabetes, the diabetes may be the result and not the cause. With such conflicting concepts regarding the damaging affects of a hyperglycemia and with so much evidence that it may be of benefit in a certain group of diabetic patients is it essential in the treatment to insist on normal blood sugar value, having rendered the urine free from sugar? The patient is the one who can best guide us in this respect. If he feels well, is able to carry on, maintains his weight and is satisfied with the dietary prescription and at the same time does not excrete sugar I do not advocate any

further dietary change or the use of insulin to reduce the blood sugar, should it be found above the accepted normal value. The argument has been advanced that it is wise to reduce the blood sugar to its normal level, regardless of the urinary findings, because it represents a physiological state. In the non-diabetic such a hypothesis is tenable. In the diabetic I feel that a moderate hyperglycemia may represent the organism's adaptation to an abnormal situation. No one will deny that a heart of normal size is most desirable but that under certain conditions its hypertrophy serves a useful purpose. This is just one of many examples of bodily adaptations to pathological states and I feel that a mild hyperglycemia is another, and should not be too zealously treated as long as the urine is free from sugar.

To summarize I conclude as follows:

1. The determination of the blood sugar is of greatest value in the *diagnosis* of diabetes mellitus. This determination is of help as a single fasting specimen or as a series of specimens following any of the tolerance tests. In the evaluation of such tests diseases of the biliary tract and the previous diets of the patient must be reckoned with.

2. A single blood sugar determination is of little value in determining the severity or prognosis of a case of diabetes mellitus.

3. In the treatment a sugar free urine is a satisfactory laboratory criterion. In the young diabetic the blood sugar will approximate normality under such conditions; in the older patient let the blood sugar seek its level, even though high. There is little evidence to prove that such a hyperglycemic state is deleterious and there is considerable evidence that it is desirable.

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Discussion

Dr. Elaine Ralli: Mr. Chairman, fellow members: I am very glad to have been asked to discuss these papers this evening and I must say it is very easy because I am in entire agreement with practically everything that the three speakers have said. I should like to stress one or two points. If I may go back to one of the points that Dr. Himwich brought out in his paper, that is the matter of dehydration. It is a peculiar thing that although dehydration has been spoken of repeatedly, Dr. Himwich showed it very beautifully here in 1933 at the Graduate Fortnight, Atchley has reported it, and Peters and his collaborators have written on the subject, that too little attention has been paid to it clinically as probably one of the most important factors in diabetic ketosis. The importance of dehydration is borne out by the fact that treatment of diabetic coma by insulin alone, although it may clear up the ketosis, will not always return the patient to a conscious state, and the additional injection of saline intravenously will bring back consciousness, which from the patient's point of view, is a very desirable state to be in. We recently had an opportunity of observing a case in which the dehydration and anhydremia were unusually severe because of a preceding period of starvation which antedated even the ketosis. The CO_2 combining power was 17.06 per cent and the blood sugar high. Here again I agree with Doctors

Tolstoi and Himwich that blood sugars are of relative importance. When treated with N/saline the patient lost a good deal of the fluid, due to the fact that the preceding starvation had reduced the level of protein in the blood, and absorption from the blood was apparently impaired. The dehydration therefore was not relieved. Following a transfusion, however, fluid was again administered, very rapidly absorbed, and the patient returned to a normal state in an amazingly short period of time, actually two hours. Dehydration with its complications is one of the primary reasons for controlling glycosuria.

The relation of glycosuria to blood sugar has been very well brought out and as I say, I am very much in agreement with what has been said. Personally, I sometimes feel that it would be wiser never to do blood sugars on diabetics, because, strangely enough, both the patient and occasionally others having taken a blood sugar, seem to think that it stays at that level until the next blood sugar is taken. The patient will constantly tell you, "My blood sugar was so many counts." Naturally, it varies a good deal during the day in normal persons and more so in diabetics, and if the patient is treated on the basis of blood sugar, overdoses of insulin are very often given, and hypoglycemia occurs which seems to me a very undesirable thing to have happen. Therefore, I would stress again what Dr. Tolstoi has said, the effort should be to maintain a sugar free urine and this will probably mean a blood sugar within fairly reasonable limits and the prevention of marked glycosuria will avoid the consequent dehydration that occurs with the loss of fluid.

If I may go back now to the first paper, I would like to speak of just one or two things, and that is the matter of infection in diabetes. I am glad Dr. Bayne-Jones brought out the fact that hyperglycemia has no effect on the increased or diminished resistance of an individual to infection. It seems to me that one forgets that the diabetic is subject to a profound disturbance of nutrition, and these elements are probably the factors which lead to a diminished ability to resist infection. I say this for two reasons:

One is that we have the experience of treating people on the Third Medical Division at Bellevue Hospital who are badly nourished and we find infection in those individuals who have been subject to a poor diet for a period of time. Secondly, because of our experience with depancreatized dogs. The depancreatized animal can be kept in a perfectly good state providing the diet is absolutely adequate. If you omit one element from the diet of this animal, its reaction is much more violent than if the same element is omitted from the diet of the normal animal. I hold no brief for the fact that vitamin A is, or is not an anti-infective vitamin. I think undoubtedly the proof is not sufficient. However, it apparently has something to do with the general state of nutrition. If a normal animal is placed on an A deficient diet, it will show certain symptoms, and it will develop certain infections sooner or later. A diabetic animal deprived of Vitamin A will show these same symptoms much more rapidly. Apparently, then, the diet influences the general state of nutrition. In a diabetic individual, particularly the one who is not controlled, the losing of valuable nutritive elements in his urine as the result of an increased loss of fluid and being on a diet that is not adequate in vitamins and minerals probably contributes to a general state of under-nutrition. Another point which brings this up at the present time is the fact Dr. Root in Dr. Joslin's clinic has shown that the incidence of tuberculosis is increasing in diabetics, and decreasing in individuals of the same age who are normal. This again I think is probably due to a poor state of nutrition in the diabetic individual, and this fortunately need not now occur, because the type of diet used in the diabetic now so nearly approaches the normal that it should contain all the elements that are required in the normal diet.

DR. H. RAWLE GEYELIN: I have enjoyed listening to the speakers of the evening. As regards Dr. Bayne-Jones' paper that the degree of hyperglycemia probably has no influence upon susceptibility to infection in diabetes, I am

in hearty agreement. It is also true that diabetics kept in ideal condition as regards freedom from glycosuria and hyperglycemia are sometimes more subject to infection than others who show constant hyperglycemia. I should like to refer to a case in point. A girl who has been well treated with diet and insulin for the past 14 years recently developed lobar pneumonia. In spite of the fact that prior to the onset of the pneumonia she was always sugar free with normal blood sugar and that this condition obtained throughout the disease, she died on the third day of a rapidly spreading pneumonia with leukopenia. During the course of her brief and fulminating infection she never showed any sugar in the urine nor hyperglycemia. In this instance, she received 200 grams carbohydrate per day with 10 units of insulin every 3 hours.

I concur with the point brought out by Dr. Ralli, and which I would like to emphasize even more than she did, namely, the fact that the incidence of infection in diabetics seems to me to be more readily affected by the nutritional state of the individual rather than by the blood sugar level. Diabetics who are adequately nourished, free from glycosuria and maintaining normal weight are less apt to have an infection than are those who are kept in moderate or extreme degrees of undernutrition. This is particularly true in the case of tuberculosis. I believe that Joslin has found that the incidence of tuberculosis in diabetes is increasing. Such is not in accord with our findings. We are seeing less tuberculosis amongst diabetics than formerly. Here again I feel that the difference of opinion is due to undernutrition vs. normal nutrition.

As I understand Dr. Himwich, he makes the point that the onset of polyuria in diabetic acidosis is primarily brought about by the excretion of ketone acids. Such has not been our experience. Polyuria in diabetics going into acidosis usually develops because of a steadily increasing glycosuria and is quite apparent before there is much ketonuria, sometimes before the appearance of any ketonuria, and as has been shown by numerous observers, dia-

betics of normal weight and strength do not develop a polyuria unless the urine contains at least 50 or more grams of sugar during a 24 hour period.

It is gratifying to hear what most of the speakers have said regarding blood sugar. I think the importance of a blood sugar test in the management of diabetics is overrated. This does not mean that I believe the test should be discarded. However, I think many of us are inclined to attach too much significance to a degree of hyperglycemia which is little above the normal level of spilling, i. e., 170 mg. Also, we must not forget that very often one blood sugar determination during a 24 hour period gives us no picture of what the blood sugar may show at every other 5 minute period of the day and night. Many times we have taken 4 to 8 blood sugars during a 24 hour period and found only one or possibly 2 above the level of 170 mg. The others have been well within the normal limits, and the patients have been sugar free in their urine.

Finally, I should like to re-emphasize the statement which I have made on other occasions and have alluded to tonight, namely, that normal nutrition by means of normal diet should be the therapeutic goal of every clinician who treats diabetes. Both overnutrition and undernutrition are to be avoided.

DR. FREDERICK M. ALLEN: Mr. Chairman, ladies and gentlemen: I am glad that Dr. Himwich is taking up the study of the partially depancreatized dog, because I have always considered it the ideal means of reproducing human diabetes. I would remind, him, however, that what I used was not the Sandmeyer preparation. In the literature he will find that the Sandmeyer procedure was to leave a portion of the pancreas to atrophy without a duct, whereas the dogs I used had a piece of pancreas connected with the bowel, so they could thus digest food and reproduce clinical diabetes very satisfactorily.

As the first speaker has stated, bacteriology does not explain the susceptibility of the diabetic to infection. On the other hand, these experiments with diabetic animals

furnish some definite information. The totally depancreatized dog is extremely susceptible to infection, so that with the cleanest laparotomy it is almost impossible to avoid peritonitis. With partial pancreatectomy, even though only one-twentieth of the pancreas be left, the diabetes may be very severe but abdominal operations can be performed with practically the same impunity as in a normal animal. Furthermore, by starving the totally depancreatized dog and by feeding or injecting sugar in the partially depancreatized one, we can produce greater glycosuria and hyperglycemia in the latter than in the former, but the difference in susceptibility to infection still persists.

With reference to Dr. Mosenthal's hypothesis and the other remarks concerning dehydration, Dr. Himwich will be able to observe that these partially depancreatized dogs can be kept for months with severe glycosuria and polyuria and evidences of the accompanying dehydration, yet they do not show the lack of resistance to infection which characterizes the totally depancreatized dogs. Also, by proper means, these partially depancreatized dogs can be thrown into acidosis and even coma, with the same profound dehydration as witnessed in human cases, and yet they do not in acidosis develop any such sensitiveness to infections as the totally depancreatized dogs. These facts do not seem to agree with the speculative explanation of susceptibility to infection, as due to dehydration. It seems to me only necessary to realize that diabetes is a specific impairment of nutrition, affecting all the cells of the body, and in this way the susceptibility to infection and all the complications and degenerations accompanying diabetes can be rationally explained. This has nothing to do with nutrition in the sense referred to by Dr. Ralli and Dr. Geyelin. The connection of infections with nutrition in that sense is contrary to fact. The fat diabetic is often the very one who develops boils, carbuncles and other infections. With undernutrition before the discovery of insulin, patients were sometimes starved down to actual emaciation, but they did not become infected. They did not have boils, carbuncles or any other diabetic complications, because their resistance was better

when they were undernourished than when they had the specific nutritive disorder of uncontrolled diabetes. The undernourished patients lacked normal resistance to tuberculosis, because of general weakness, but they had better resistance even against this disease than diabetics on high diets with high sugar analyses.

With reference to pluriglandular speculations, it should be remembered that the blood sugar in typical hyperthyroidism is normal, and diabetes has never been proved to result from disorder of any gland or combination of glands in the presence of a normal pancreatic island function; furthermore, the great mass of diabetic patients whom we are called upon to treat do not show the slightest evidences of thyroid, adrenal or pituitary disturbance, and when disorders of these other glands co-exist they represent recognizable complications.

Under the arrangement of this program it is scarcely possible that I, as the only advocate of a normal blood sugar, should attempt in five minutes to answer a whole array of speakers on the opposite side. I am even led to suspect that Dr. Mosenthal may possibly have had something to do with the make-up of this program. If I could have an equal amount of time with the other speakers, I should be very glad on any evening to discuss with them in detail the various points which they have raised. At present I can only suggest that the numerical disproportion of enthusiasm for abnormal blood chemistry on this evening's program by no means corresponds to the weight of opinion among either diabetic specialists or the general medical profession, and I must take comfort from the words that were spoken to the prophet of old: "Fear not; they that are with thee are more than they that are against thee."

If the facts, either physiologically or clinically, were so clearly in agreement as the speakers this evening would represent, it seems strange that Dr. Joslin, for example, should in his book advocate the maintenance of normal blood sugar. Similarly, Dr. Hagedorn and his collaborators, who seem to have made the latest important contribution to diabetic therapy, lay stress on a normal blood

sugar as the ideal of treatment. I myself, when a patient comes to me with an abnormal condition, feel that I can render him no greater service than to restore him as nearly as possible to normal, and I do not aspire to improve upon nature. From the treatment of a few thousand diabetics, I can testify that there is no particular difficulty in keeping the blood sugar within an approximately normal range, except in a small number of cases; furthermore, there is no great hardship on the patients. I have never seen a single instance of harm from this policy. I think I have seen benefits. I know this: that in a few instances of long standing diabetes I have seen typical complications, of retinitis and gangrene, which developed at a time when there was high blood sugar without any sugar in the urine, and which subsided with the mere reduction of the blood sugar. The idea of the benefit of high blood sugar, especially in heart disease, is based, it seems to me, upon a curious misconception of both physiology and medicine; namely, upon the idea that a high blood sugar due to impaired utilization of sugar is equivalent to the high blood sugar created by intravenous injections in the presence of normal utilization. The benefit is in the utilization, not in the flowing of sugar past the heart cells without utilization. I agree that certain patients with coronary disease may die from insulin reactions, and it is therefore inadvisable to proceed rashly in such cases. But it is not necessary to proceed rashly. I agree thoroughly with Dr. Joslin and others who say that the very fact that the heart is diseased creates all the greater necessity of aiding it by making the utilization of sugar as nearly normal as possible.

As there is no time for further details, I wish to close with just two questions. First, we have been speaking about partially depancreatized dogs. Would the advocates of high blood sugar in heart disease wish to partially depancreatize their cardiac patients, in order that they might have the benefits of a continuously elevated blood sugar due to slightly impaired utilization? Second, I have referred to Dr. Hagedorn's protamine insulinate, which I have been privileged to begin using, in the hope that it will provide

a more efficient means of regulating the blood sugar. Suppose that this regulation can be carried further, so that we shall be able easily to maintain any desired level of blood sugar. Suppose that the progress extends still further, so that we are offered an actual cure of diabetes, with the necessary result of a return of the blood sugar to normal. Will the advocates of high blood sugar reject such therapeutic procedures, in order that their patients may continue to enjoy the benefits of hyperglycemia?

DR. HERMAN O. MOSENTHAL: It is perfectly true that I invited the speakers to come here tonight. On the other hand, there were only three whose views I knew, Dr. Ralli and Dr. Allen; the third one I thought sided with Dr. Allen —at least he told me so fifteen years ago when we discussed this subject. Apparently he has changed his point of view since then.

I was very anxious to have as the objective of this meeting the presentation of the unbiased thought of men who were well-versed regarding infections, who knew about the experimental side of diabetes, and those who were experienced clinicians. Our speakers and discussors have told us from their point of view what is presumably correct. It is obvious that if we have a means for regulating the blood sugar no physician is going to avoid maintaining a normal blood sugar level in his patients. On the other hand today we are less able to control glycosuria and blood sugar than many would lead us to believe. The textbooks on diabetes and the dictum of various diabetes specialists are distinctly at fault when they state that a normal blood sugar is readily achieved and easily maintained.

The two recent articles from Denmark and Boston, describing the experience with the new insulin product, acknowledge the really existing state of affairs.

The problems we have to solve as best we can are:

Is hyperglycemia in the absence of glycosuria harmful?

Is it advisable to stress a normal blood sugar at the risk of hypoglycemic reactions?

Is a high blood sugar at times beneficial and in some cases even a necessity?

Hypoglycemia is a most devastating condition and fraught with a good deal of danger to the individual. I try to avoid such reactions whenever possible in my patients, and it was to obtain the justification of this practice that I have been so interested in finding out whether or not a hyperglycemia was harmful.

A clinician is perfectly justified in basing his conclusions largely on his clinical experience. My observations lead me to believe that hyperglycemia without glycosuria does not harm the patient. This idea was originally developed in the pre-insulin period when there were many cases of infection in whom nutrition was of paramount importance. Those cases who received a high diet but not sufficiently high in carbohydrates to produce glycosuria, had their carbuncles, furuncles and infections heal very neatly provided the urine was sugar-free although the blood sugar would be high.

I have yet to see a case of diabetic gangrene, cataract or arteriosclerosis where there has not been a preceding period of at least five years in which the diabetes has been carelessly treated; that is one in which there has not been a persistent glycosuria for at least five years. This would indicate that glycosuria and polyuria, that is malnutrition and desiccation, are the causes for complications in the diabetic and not a hyperglycemia without glycosuria.

Closing Discussion

Dr. Edward Tolstoi: Dr. Mosenthal had me in mind when he referred to one of the speakers who concurred with Dr. Allen's viewpoint fifteen years ago but who has changed his mind. I sincerely hope that Dr. Allen does not think me too ungrateful because all my preliminary training and basic training in diabetes has been given me by Dr. Allen and I am extremely grateful to him for all of it. I hope he does not think the worm has turned. It is just an evolution of a viewpoint that came upon me from observing a very large number of cases and following those cases very care-

fully that I came independently, I may say, to some conclusions of Dr. Mosenthal and the other speakers of the evening here. I have one or two remarks that occurred to me when Dr. Allen raised certain objections. I will not take up too much time, but I want to reemphasize certain things I have said probably for clarity. Dr. Allen stated in the totally depancreatized dog infections supervene while in the dog where even one-twentieth of the pancreas is left, you can operate and have no fear that infection will appear there as readily as in the totally depancreatized dog.

How does that, ladies and gentlemen, apply to pancreatic human diabetes? Do we ever see a case of total pancreatic diabetes in the patient? That is an extreme rarity. I recall only one case in the literature. I don't know how definitely established that was. It is the famous case of Cyril K. We don't see cases of total diabetes. We see some infections, but I don't think, as I stated, they are much more prevalent in these patients than they are in the normal run of people. We are terribly impressed and profoundly so, when the patient sent to us from the skin clinic because of boils or carbuncles reveals a glycosuria, and there is the answer. We immediately connect diabetes with infection. But we forget the case of furunculosis which comes to us and which presents no glycosuria. That just happens to be a case of furunculosis and we let it go at that.

Dr. Allen also states that a fat diabetic may show boils. That is very true. I feel in those cases it is not only the diabetes, it is the diabetes and something else. We see that in the older patient and I feel that patient also has vascular lesions.

Gangrene and retinitis. If diabetes or hyperglycemia were responsible for gangrene or retinitis, why is it so infrequent in the young where diabetes is most usually severe. I have asked myself that question repeatedly, and I have yet to find a satisfactory reply. Gangrene and retinitis occur in people who have vascular disease, and whether the diabetes precedes or follows the vascular disease, I am in no position to state, but they are always

found in pairs. That is our experience in the clinic, when we see retinitis we see vascular change in the eye. Furthermore, we refuse to call them diabetic retinitis. It is vascular disease. We see the same type of disease in the eye-grounds of some hypertension patients.

Dr. Allen's point, why not treat heart disease by removing the pancreas. Dr. Marvin at New Haven has reproduced that but in a simpler way. He prefers to give his coronary cases glucose intravenously. Tides them over the acute period, and then treats them by the routine method.

ERRATA — FELLOWSHIP LIST

ANNUAL REPORT FOR 1935, PUBLISHED IN APRIL, 1936

Through an error the name of Dr. Martha Wollstein, a Fellow of the Academy since 1901, was omitted from the list of Non-Resident Fellows. Dr. Wollstein is at present in Grand Rapids, Michigan.

The following are the corrected degrees of Dr. Russell Henry Chittenden of New Haven, Honorary Fellow of the Academy: Ph.D., Sc.D., Hon. M.D., LL.D.

THE MARTLAND LECTURES

Dr. Harrison Stanford Martland—An Appreciation*

Emanuel Libman
New York

It is to me a much appreciated privilege to make some introductory remarks on this occasion. Tonight the Essex County Anatomical and Pathological Society inaugurates the Harrison Stanford Martland Lecture, in honor of our friend. It is not usual for a man to be thus honored during his lifetime, and at so early an age. We who know Martland realize that he is richly deserving of the attention that is being shown him.

The course of his medical life has been a rather simple one. After graduation from the College of Physicians and Surgeons, New York, in 1905, he was an interne at City Hospital on Welfare Island for eighteen months. He then spent a period of two years in pathology and bacteriology at the Russell Sage Laboratory. In 1909 he became pathologist to the Newark City Hospital. Until the institution was rebuilt, he worked under most primitive conditions. Since 1925 he has been Chief Medical Examiner of Essex County. He became Associate Professor of Forensic Medicine at the New York University College of Medicine two years ago, and it is expected that he will soon occupy the full professorship formerly held by Dr. Charles R. Norris, to whom he was always so devoted.

Dr. Martland entered the Army in 1917 as a member of the Bellevue Hospital Unit. His services were so distinguished that he was made a Colonel in the Reserve Corps in 1919, and that the Rockefeller Foundation desired him for the directorship of an Institute of Hygiene, to be established for the Government of Mexico.

With such a comparatively simple training has Martland reached his high place among the medical investigators and leaders of the country. What I have already said indicates

* An address delivered on December 14, 1935, at the first Harrison Stanford Martland lecture under the auspices of the Essex County Anatomical and Pathological Society.

that he is a self-made man. He did not need teachers for any length of time. He enjoyed no privileges—he would not want them.

For many years, until 1925, he made but few publications. Since then, there has issued from his pen a series of valuable papers, the most significant being his already classical contributions on the results of intoxication by radioactive substances. Next in importance, perhaps, is the original work on punch drunk, which appeared in 1929.

It is perhaps fortunate that he wrote so little for the first sixteen years of his work here (there is a period of seven years—1909 to 1916—with no publications). He was soaking in valuable observations first hand, at the post-mortem table and in the laboratory. He did not have to confine himself to one or a few subjects. As a result, we find him equally at home in morbid anatomy, pathological histology, forensic medicine, bacteriology, and clinical laboratory methods. As I stated on another occasion, Martland is a master in pathology and a master in forensic medicine. His knowledge of hematology is extraordinary. He has command of and has made good use of the experimental method.

The museum of the City Hospital, built up by him, is one of the most valuable in the country. Dr. Martland does practically all of the work himself. He makes his own drawings and illustrations. He has the knack of demonstrating what is to be shown, and very clearly. The atmosphere of his laboratory is that of a university, and not that of the usual municipal hospital.

Martland is an unceasing worker. There is no difference, in his laboratory, between weekdays and Sundays, or work days and holidays. Even today, the best chance of finding him late at night is at the laboratory. It has always been a mystery how he succeeds in doing so much, and how it is that his loyal, sterling associates have not succumbed.

To make the situation more remarkable, he finds time for extensive court work, preparation of numerous papers, appearances at medical meetings, crime conferences, etc., and for much activity on behalf of the New York Academy

of Medicine. There he is Secretary of the Committee on Admission and Director of the Scientific Exhibits for the Graduate Fortnights. I need not tell you what he has done for the Fortnight—the fame of the exhibits is widespread. The Academy and the profession at large are under a real debt to him.

As a teacher, Martland is outstanding and *sui generis.* Not given to formal methods, he is a great teacher. In fact, he cannot help imparting knowledge. After years of almost complete silence, he has begun to teach in connection with exhibits. He has given may exhibits of his own observations and studies at the Academy and at numerous meetings, especially of the American Medical Association and your own State Society. You cannot be in Martland's laboratory for five minutes without learning something. I have often looked forward to spending some months following him about, in order to imbibe some of his large store of special knowledge.

Dr. Martland could have done formal teaching, for he has refused a number of important academic positions, some already offered many years ago. But he is too much attached to his work here, his home city, to have any willingness to go elsewhere. The only possibility of his being taken away, I believe, would be the creation of a medicolegal institute which would serve as a center for education in forensic medicine for the country at large, and which could lead to a wiping out of the obsolete coroner system, still so prevalent. The acceptance of such a post he would look upon as a solemn duty. And it may be said truly, that in the present generation, the future of forensic medicine in this country is dependent upon Martland more than upon any other man.

There is much to say of Martland, the man, but it is unnecessary that it all be told on this occasion. For you are his associates and friends, and there must be good reason why you all, close to him for so many years, love him—and why Dr. Welch, after attending one of his demonstrations at the New York Academy of Medicine, wrote to me, "Martland is a joy to meet."

I would like to say something of a few qualities of Dr. Martland. First, his naturalness, and his love of the truth. He knows the truth in a medical problem, and knows it in relation to human beings. I have never heard him tell even a "white lie," and you know how rare such beings are. Then comes his modesty. I cannot resist telling a significant story about that. On October 8, 1925, when he was scheduled to speak on his work on intoxication by radioactive substances at a meeting of the New York Pathological Society, he was accompanied by his and your friend Staehelin. You all remember Staehelin, that scholarly man, that beautiful character. When they arrived in New York Martland wanted to return to Newark, because he felt that his work was not worthy of presentation. I was ill at the time. Under the guise of a sick call, Staehelin induced him to come to my home. It was only with the greatest pressure that we succeeded in getting him to go to the Academy, where his work was acclaimed.

It is not generally known that Martland manages to find time for some clinical work and that he is an able clinician, with a fine knowledge of electrocardiography, roentgenological diagnosis, and other accessory clinical methods. You men of Essex County have for years been going to him for advice as to your cases. You have also gone to him for advice in your difficulties, and have indeed made him your leader in all things. And here we have the essence of all that Martland has, is, and will be doing for all the years to come. The secret of Harrison Martland's influence lies in his love for his fellow men. He knows superiors, but recognizes none as inferiors.

Members of the Essex County Anatomical and Pathological Society: You have done a fine deed in establishing the Harrison Stanford Martland Lecture. You have honored the community and yourselves by the respect that you show to a worthy comrade. By the choice of the first lecturer, you have indicated in what high regard the Martland Lecture will be held by you. I congratulate Martland and you, and extend my best wishes for all your future activities.

Introduction of George Hoyt Whipple, M.D.*

Frederic Sondern
New York

There are few as well suited for the introductory "Harrison S. Martland Lecture" as the guest speaker of the evening. The Essex County Anatomical and Pathological Society is indeed fortunate both in the selection of the man whose name is honored by this group of lectures and the first essayist of this series.

George Hoyt Whipple was born in that part of New England noted for intrepid men, of whom Calvin Coolidge was an example.

He came out of Yale University a Doctor of Philosophy, a college whose graduates with that degree rank foremost both in science and industry. His medical education was obtained at Johns Hopkins at a time when that mentor William H. Welch was the life of pathology in this country and its most worthy exponent as the basis of scientific medicine. To mention "Popsie" Welch is to think of him that intimately, and to suppress a pang at the recollection of his passing. It reminds me of a birthday celebration of his, I think it was the eightieth, which was sponsored by President Hoover in Washington. Two addresses on that occasion stand out in my memory. One, Simon Flexner's eulogy on Welch's personal magnetism and modesty, his scientific profundity and his teaching ability. The other, Dr. Welch's response, replete with gratitude to his own teachers abroad coupled with the hope that he had emulated them at home. George H. Whipple is the proof that he did. A favorite student and later the assistant of Welch, inspired early by that master teacher to interest in pathology, he is devoting his life to it. The bone marrow, the liver and the blood are the favorite subjects of his research activities.

After leaving Hopkins, the Ancon Hospital under Gorgas, and the Bayside Hospital in Baltimore, he became professor of research medicine at the University of Cali-

* Dr. Whipple is Dean of the Medical School of the University of Rochester, and was the first lecturer in the Harrison Stanford Martland Series, under the auspices of the Essex County Anatomical and Pathological Society, on December 14, 1935.

fornia, and after that was called by Mr. Eastman and President Rush Reese to the University of Rochester in similar capacity.

Today he is Dean of the Rochester School of Medicine and the Professor of Pathology. As Dean the results show his success, doubtless based in part on the precepts of Welch. His able and magnetic teaching is shown by the fact that each of six of his classmates at Hopkins has sent a son to study with him in Rochester. As research worker his is today a master mind, proven by the award to him of the Nobel prize in 1934.

We are honored, Sir, by your presence, and it is my privilege to present you to this company, Dean Whipple of the University of Rochester.

Problems in Anemia*

George Hoyt Whipple
Rochester, N. Y.
Dean of the Medical School of the University of Rochester

In developing his subject, "Problems in Anemia," Dr. Whipple reviewed his experimental work on anemia in dogs, due to loss of blood, which was begun in 1908. The study of hemoglobin regeneration was undertaken as an offshoot of the study of bile pigment metabolism. Dr. Whipple showed lantern slides illustrating the influence of various dietary substances on the regeneration of hemoglobin in the dog, and as early as 1920 demonstrated that liver has a powerful effect upon hemoglobin regeneration. The observations of Dr. Whipple on the influence of liver and various dietary substances on hemoglobin regeneration led to the use of these substances in the treatment of human anemias.

Dr. Whipple then reviewed the role of iron and its utilization in experimental anemia. He showed that iron given intravenously to standard anemic dogs, in large or small doses, will be returned quantitatively as new-formed hemoglobin on the basis of ten milligrams of iron equaling three grams of hemoglobin.

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* An abstract of the scientific lecture in the first Harrison Stanford Martland series under the auspices of the Essex County Anatomical and Pathological Society, on December 14, 1935.

When iron is given by mouth to these standard anemic dogs, the influence on hemoglobin production is not proportional to the amount of iron administered. An optimum dose of iron (40 mg. iron per day for two weeks, or 560 mg.) will give a net output of about 55 gm. hemoglobin, and this means about a 35 per cent utilization of the iron given. With larger doses the hemoglobin output increases a little, and with 400 mg. iron daily the net output would average about 95 gm. hemoglobin, or about a 5 per cent. utilization of the iron given by mouth.

Iron contained in salmon bread under certain conditions may be utilized by these anemic dogs up to about 40 per cent. to produce hemoglobin. Iron in the normal liver when fed may show a 45 per cent. utilization of this tissue iron.

When liver feeding is combined with iron feeding, there is a definite summation effect.

When intravenous iron in large doses is combined with liver feeding or iron by mouth, there is no evidence of summation. This probably means that the top functional capacity of the body to produce hemoglobin has been reached,—about 10 gm. hemoglobin output per day.

Iron salts are utilized with equal facility by the dog to produce hemoglobin when given by mouth in the ferrous, ferric, or reduced state. The determining factor is the amount of the iron metal.

The Eck fistula and splenectomy lessen the capacity of the anemic dog to conserve and utilize iron given by vein to produce new hemoglobin.

Dr. Whipple showed that in experimental animals the reserve iron storage can be exhausted during two or three months by a continuous anemia with the hemoglobin level maintained at one-half to one-third of normal. In animals so depleted, Dr. Whipple traced the fate of iron given by mouth or vein.

A rapid turnover of iron is the conspicuous feature of the experiments dealing with iron given by mouth and short feeding experiments (one or two days) give no evidence

of any iron store in the liver. As the iron feeding experiments are lengthened, we see a variable accumulation of iron in the liver, but the amounts are small and a very rapid appearance of the iron in matured hemoglobin is the conspicuous feature.

The importance of blood-free organs is stressed, and other method difficulties are discussed.

Parenchyma iron of various blood-free organs is relatively a constant in these dogs. Liver, kidney, and pancreas average 1 to 2 mg. per 100 grams of iron; the lung is a little higher, or 3 mg.; the spleen is still higher, or 5 to 6 mg. The red marrow apparently has the highest level of parenchyma iron—an uncertain figure, but probably in excess of 10 mg. Fe per cent per 100 grams of iron. The striated muscles actually rate with the liver and kidney, although the average for total contained iron is 3.1 mg. per 100 grams of iron. About 1.6 mg. iron is muscle hemoglobin iron, leaving the parenchyma iron as 1.5 mg.

Muscle hemoglobin iron and muscle parenchyma iron are inviolate stores of iron which are not drawn upon no matter how great is the emergency due to anemia. Conversely no surplus iron can be demonstrated in this tissue where iron is given intravenously.

Iron depletion can be carried to a point where there is almost a complete cessation of hemoglobin production in a standard dog on a diet very poor in iron.

Intravenous iron in the doses given will result in large storage in the liver and spleen—55 to 70 per cent of the total iron given. We are not prepared to say where the remaining iron is to be located in the body tissues or fluids, but it certainly is not eliminated.

In his early work, Dr. Whipple noted that dogs with abnormal conditions such as acute and chronic infection, and liver injury, did not regenerate hemoglobin to the same extent as dogs without these abnormal states. Later experiments about to be published elsewhere demonstrate that infection disturbs the utilization of iron and accounts for the failure of iron therapy in anemias due to infection.

BOOK REVIEW

THE JEFFERSON-WATERHOUSE CORRESPONDENCE ON VACCINATION*

1800-1803

From most casual beginnings we now have in orderly arrangement, with scholarly background and direct documentary evidence, a charming and vivid story of the vicissitudes, and triumph in this country of the most nearly perfect public health procedure in all history.

An idle but inquisitive moment at Charlottesville, Va., tempted our colleague, Dr. Halsey, to follow the dusty trail of forgotten letters from and to the most intellectually gifted of our Presidents, and to and from that remarkable, imaginative, yet critical and tenacious physician, Dr. Benjamin Waterhouse of Boston.

After a brief biographical sketch of the two correspondents, so far as necessary to involve them and their families in the conspiracy to test, prove successful and promote vaccination with the "kine-pox" in the states of the nation, Dr. Halsey reveals the trials of the outlander who intrudes upon the complacent competence of Boston's medical and social circles with heterodox ideas and proposals.

From that day in June, 1800, when some "matter" was received from Dr. John Haygarth of Bath, until March 1, 1803, we can follow the course of progress from doubt and distrust to international acceptance of the safeguarding inoculations.

The President and Dr. Waterhouse, and Dr. Jenner and some of his British contemporaries all discuss in the quoted letters, with reason, insight and public spirit, the implication, hopes, hazards and ultimately convincing proofs involved in the trial and practice of vaccination.

Justly and with good cause does our practitioner historian of today pay tribute in his closing paragraph to the

* Halsey, R. H. *How the president, Thomas Jefferson, and Doctor Benjamin Waterhouse established vaccination as a public health procedure.* New York, The Author, 1936. (History of medicine series, issued under the auspices of the Library of The New York Academy of Medicine. No. 5.)

notable leadership of the zealous though never fanatical Dr. Waterhouse:

> "To Dr. Waterhouse is due, therefore, the credit of devising the method, and inviting Jefferson to lend his influence in the execution of the procedure and thus expediting the introduction of vaccination as a preventive of smallpox and establishing it as a recognized public health measure."

HAVEN EMERSON.

RESOLUTIONS OF THE COUNCIL PASSED APRIL 22, 1936, ON THE DEATHS OF ARTHUR B. DUEL AND HARLOW BROOKS

ARTHUR BALDWIN DUEL

The Council of The New York Academy of Medicine records with deep feeling its sense of loss in the death on April 11, 1936 of Dr. Arthur B. Duel who for many years had been a member of the Council.

Dr. Duel was elected a Fellow of the Academy in 1899. At that time, he was actively interested in everything pertaining to the advancement of the practice of medicine. He was engaged in hospital work, particularly in the field of otolaryngology and did much toward raising the standards of practice in this field. He was not satisfied with being a local influence only, but rapidly took his place as a leader nationally and internationally. His work in connection with the repair of the facial nerve done in association with Sir Charles Ballance was of the highest scientific order and gained him an international reputation.

With these many activities, he never failed to carry his responsibilities as a Fellow of the Academy in full measure. He was one of those who early visualized the enlarged usefulness that the Academy might attain. It was by his efforts that one of the major contributions was secured which enabled the Academy to own and work in its present beautiful home. For this work to be effectively carried forward, it was necessary that a man of outstanding ability and experience be secured as its Director. It was Dr. Duel who recognized in Linsly Williams a man specially quali-

fied for this position, and the record made under Dr. Williams' administration is well known.

As a member of the Council, during the years he was a Vice-President, and as a Trustee, Dr. Duel was unfaltering in his continued interest, wise counsel and active work.

The Academy through its Council records the deep sense of loss that has been sustained—a loss which is felt as a personal one by all those who were associated with Dr. Duel in his work.

The Council orders that this resolution be spread upon its minutes and a copy thereof presented to his family.

Harlow Brooks

Dr. Harlow Brooks died on April 13, 1936 in the very height of his professional activity. In his death, The New York Academy of Medicine has suffered an irreparable loss.

Throughout his life he was one of the outstanding men of his profession in the fields of general medicine and medical education.

He was elected a Fellow of the Academy in 1904 and from the very first became a dominant factor in its work. Dr. Brooks was particularly interested in the education of the general practitioner. He devoted a major portion of his time to teaching in the hospitals and medical colleges. His following was very large and very personal. His personality impressed itself upon those with whom he worked and scores of physicians are more capable because of what they learned from Dr. Brooks.

He accepted with real seriousness his responsibility as a Fellow of the Academy, served on many of its committees, became Chairman of the Committee on Medical Education, and was elected a Vice-President in 1932. In all of these positions, he gave freely of his time and his matured judgment in advancing the interests of the Academy and through it of the medical profession. Those who were intimately associated with him in this work feel a deep sense of loss which it is difficult to express.

The Council of the Academy records its great appreciation of his accomplishments and its sorrow in that the Academy is to be deprived of his services and engaging personal association. It is ordered that this resolution be spread upon the minutes and a copy thereof presented to his family.

ARTHUR BALDWIN DUEL
1870 - 1936

Arthur Baldwin Duel died at Laurelwood, his country place near Pawling, New York, on the eleventh of April last. He was born at Granville, New York on December 14, 1870 and was educated in its preparatory schools and at the University of Vermont. He then entered Harvard Medical School from which he graduated cum laude in 1894. After a year's interneship at the Boston City Hospital he came to New York and joined the surgical staff of the Manhattan Eye, Ear and Throat Hospital in November, 1895. At this time he did work in pathology at the New York Post Graduate Hospital and was from 1896 until 1900 connected with the Aural Department of The New York Eye and Ear Infirmary. He was for some time Professor of Otology at the New York Polyclinic Medical School and Hospital, and at the time of his death was Senior Aural Surgeon, Chairman of the Board of Surgeon Directors and Vice-President of the Manhattan Eye, Ear and Throat Hospital. He was Consulting Otologist to the New York Board of Health and the Willard Parker Hospital, The Babies Hospital, The New York Skin and Cancer Hospital and The Englewood Hospital at Englewood, N. J. He was elected to Fellowship in The New York Academy of Medicine in 1899 and was Secretary of its Section of Otology in 1903 and Chairman of that Section in 1908; Chairman of the Building Committee from 1923 to 1933. He was Vice-President in 1922 and 1923 of The New York Academy of Medicine and Trustee from 1924 until the time of his death; a former President of the American Otological Society and Chairman of its Research Committee for Otosclerosis; former President of the New York Otological Society, Fellow of the International Collegium Otolaryn-

gologicum, and Honorary Fellow of the Société de Laryngologie des Hôpitaux de Paris, Fellow of the American College of Surgeons, The American Laryngological, Otological and Rhinological Society and the American Medical Association and State Societies.

He made many contributions to Otological literature and contributed "Otology" to Progressive Medicine 1907-14, "Otology" in Billings-Forsheimer's Therapeusis of Internal Disease (George Blumer edition) 1924.

His last and chief work was begun in collaboration with Sir Charles Ballance in 1930 for the relief of Facial Palsy. Through appropriations from the Carnegie Research Fund and through the generosity and loyalty of his friends and former patients a laboratory was established at his country place where for several years the experimental research was carried on which ultimately led to the operation for decompression of the facial nerve in certain cases of paralysis and for the use of autoplastic nerve grafts in others where a portion of the nerve had been destroyed. He was called to describe his work before the scientific societies of his specialty in this country and abroad. In Brazil he was accorded Honorary Membership in the Assocao Paulista de Medicina at Sao Paulo, and he presented his work as a member of the International Collegium Otolaryngologicum at Stockholm. He also responded to an especial invitation to lecture before the Royal College of Surgeons in London and to demonstrate his operation in several hospitals in England.

He was untiring in his work and unsparing in his efforts for the advancement of Otology, and his interest in both its clinical and laboratory study was an inspiring aid to his hospital associates and to his fellow members in the councils of the Scientific Societies to which he belonged.

His strength of character, sound judgment and conscientious devotion to his work was combined with rare generosity of spirit and personal charm. His memory is cherished by all who worked with him and learned from him, and by hundreds who are grateful to his unfailing kindness and skill.

JOHN RANDOLPH PAGE.

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London, Milford, 1936, 188 p.

MEMBERS ELECTED MARCH 5, 1936

Joseph Edward Corr.....4 East 88 Street
A. Parks McCombs.....147 East 50 Street
Norman Plummer.....140 East 54 Street
John Philip Stump.....140 East 54 Street

MEMBERS ELECTED APRIL 2, 1936

Ralph L. Barrett.....59 East 54 Street
Truman Leo Boyes.....245 East 72 Street
Norton Sager Brown.....16 East 90 Street
Julius P. Dworetzky.....7 Law Street, Liberty, N. Y.
William J. Hoffman.....410 Central Park West
Victor Clarence Jacobsen.....51 First Street, Troy, N. Y.
Ernst Friedrich Muller.....255 East 22 Street
Arthur J. Murphy.....897 Park Avenue
Jacob Werne.....89-04 148 Street, Jamaica, N. Y.

PROCEEDINGS OF ACADEMY MEETINGS

MARCH

STATED MEETINGS

Program arranged in cooperation with the
SECTION OF HISTORICAL AND CULTURAL MEDICINE—March 5

I. EXECUTIVE SESSION—a. Reading of the minutes; b. Election of Members.

Scientific Program

II. PAPERS OF THE EVENING—a. William Cheselden, some of his contemporaries and their American pupils before the Hunters, Francis R. Packard, Editor, Annals of Medical History; Discussion: Fenwick Beekman; b. The medical work of the Knights of St. John of Jerusalem, Edgar Erskine Hume, Librarian, Army Medical Library; Discussion: James J. Walsh.

III. EXECUTIVE SESSION—SECTION OF HISTORICAL AND CULTURAL MEDICINE—a. Reading of the minutes; b. Report of Nominating Committee.

THE HARVEY SOCIETY (*in affiliation with* THE NEW YORK ACADEMY OF MEDICINE)
March 19

THE SIXTH HARVEY LECTURE, "The Influenzas of Swine and Man," Dr. Richard E. Shope, Associate Member, Department of Animal and Plant Pathology, The Rockefeller Institute, Princeton.

SECTION MEETINGS

SECTION OF DERMATOLOGY AND SYPHILOLOGY—March 3

I. READING OF THE MINUTES.

II. PRESENTATION OF CASES—a. New York Polyclinic Hospital; b. City Hospital; c. Miscellaneous cases.

III. DISCUSSION OF SELECTED CASES.

IV. EXECUTIVE SESSION—Appointment of Nominating Committee.

COMBINED MEETING OF THE NEW YORK NEUROLOGICAL SOCIETY and the SECTION OF NEUROLOGY AND PSYCHIATRY—March 3

I. PAPERS OF THE EVENING—a. A pathognomonic encephalographic sign of chronic subdural hematoma, Cornelius G. Dyke; Discussion: S. P. Goodhart, E. A. Friedman; b. The treatment of obstructive hydrocephalus by third ventriculostomy. Report of two cases, John E. Scarff; Discussion: Byron Stookey, Foster Kennedy; c. On the site of action of acetylcholine and its significance, Harold G. Wolff (by invitation); Discussion: James McKeen Cattell, Frank Pike, Byron Stookey, Smith Ely Jelliffe, Joshua Leiner, Foster Kennedy; d. Varieties of aggression in parenthood, Gregory Zilboorg; Discussion: Smith Ely Jelliffe, Bernard Sachs, Reuben Gerber.

II. EXECUTIVE SESSION—Section of Neurology and Psychiatry—Appointment of Nominating Committee.

SECTION OF SURGERY—March 6

I. EXECUTIVE SESSION—a. Reading of the minutes; b. Appointment of Nominating Committee.

II. CASE PRESENTATIONS—a. Compound fracture of the skull, six months after injury; b. Compound fracture of the tibia and fibula, six years after injury, Henry H. Ritter; c. Fracture of humerus through an area of osteomyelitis, A. O. Wilensky; Discussion: J. R. Lincoln, W. T. Doran, R. Kennedy.

III. PAPERS OF THE EVENING—a. Osteomyelitis of the skull, Joseph E. J. King; Discussion: W. T. Doran; b. The treatment of osteomyelitis, A. O. Wilensky; Discussion: J. R. Lincoln, Kenneth Lewis, H. H. Ritter; c. The management of compound fractures, Henry H. Ritter; Discussion: Frederic Bancroft, Kenneth Lewis, Henry Ritter; d. Osteomyelitis in compound fractures, Robert H. Kennedy; Discussion: Frederic Bancroft, Kenneth Lewis, Henry H. Ritter.

IV. GENERAL DISCUSSION.

SECTION OF OPHTHALMOLOGY—March 16

INSTRUCTIONAL HOUR, 7:00-8:00 p.m.—Etiology and non-operative treatment of glaucoma, Mark J. Schoenberg.

SLIT-LAMP—Demonstration of cases, 7:30-8:30 p.m.—Milton L. Berliner, Girolamo Bonaccalto, Gordon M. Bruce, Wendell L. Hughes.

EXHIBIT, 7:30-8:30 p.m.—"The Embryology of the Human Eye," Brittain F. Payne (by invitation).

Scientific Program

I. Executive Session—a. Reading of the minutes; b. Election of Member of Advisory Committee (for one year and two months) to fill the unexpired term of Herbert W. Wootton, resigned. Nominee: Clyde E. McDannald; c. Appointment of Nominating Committee.

II. Presentation of instrument—an improved perimeter—campimeter, Joseph I. Pascal (5 minutes), (by invitation).

III. Report on exhibit on the embryology of the eye, Brittain F. Payne (10 minutes).

IV. Case Presentations—a. The Young ptosis operation—report of a case, Willis S. Knighton (5 minutes); b. Bilateral cyst of the vitreous—report of a case, Charles A. Perera (10 minutes), (by invitation).

V. Paper of the Evening—Orbital tumors, C. S. O'Brien (20 minutes), Iowa City, Iowa (by invitation); Discussion: John M. Wheeler, Bernard Samuels.

JOINT MEETING—SECTION OF MEDICINE and the NEW YORK HEART ASSOCIATION

March 17

I. PAPERS OF THE EVENING—a. The management of rheumatic heart disease, Lucy Porter Sutton (40 minutes); Discussion: Homer F. Swift (7 minutes), Irving R. Roth (7 minutes); b. The clinical significance of the measurement of circulation time, Arthur M. Fishberg; Discussion: Harold G. Stewart.

II. EXECUTIVE SESSION—Section of Medicine—Appointment of Nominating Committee.

SECTION OF GENITO-URINARY SURGERY—March 18

I. EXECUTIVE SESSION—a. Reading of the minutes; b. Appointment of Nominating Committee.

II. PRESENTATION OF CASES—a. Neuro-fibromatosis of the bladder and prostate. Case report, C. H. McDonnell, Ann Arbor, Mich. (by invitation); b. Transurethral resection of bladder tumors. Case reports, John A. Taylor.

III. PAPERS OF THE EVENING—a. The ectopic ureteral orifice; A study of fifteen cases in children, Meredith F. Campbell; b. Clinical and experimental study of lithotripsy, Francis Patton Twinem; Discussion by: Simon A. Beisler, Paul M. Butterfield, Abraham Hyman.

IV. GENERAL DISCUSSION—Henry Dawson Furniss, Russell Ferguson.

SECTION OF OTOLARYNGOLOGY—*Program presented in conjunction with* THE SECTION OF OTOLARYNGOLOGY OF THE PHILADELPHIA COLLEGE OF PHYSICIANS—March 18

I. READING OF THE MINUTES.

II. PRESENTATION OF CASES AND NEW INSTRUMENTS—a. Laryngectomized patients phonating without mechanical aid, George Renfrew Brighton; b. Nerve stimulator, Edmund Prince Fowler; c. Demonstration of new type of tracheotomy tube, John S. Mikell (by invitation).

III. CASE REPORTS—a. 1. Cyst of larynx, 2. Actinomycosis, John Devereux Kernan; Discussion by Louis Henry Clerf (by invitation); b. Congenital stenosis of larynx, George Hunter O'Kane (by invitation); Discussion by Chevalier Lawrence Jackson (by invitation).

IV. PAPERS OF THE EVENING—a. Non-malignant tumors of larynx, George Renfrew Brighton, Sylvester Daly (by invitation); Discussion by Gabriel Tucker (by invitation); b. Radiotherapy in otolaryngology, Maurice Lenz; Discussion by Eugene Percival Pendergrass (by invitation); c. Acoustic neuromas, Edmund Prince Fowler, Jr. (by invitation); Discussion by Benjamin Harrison Shuster (by invitation).

V. GENERAL DISCUSSION—Clinical demonstrations and lectures were held at The Columbia Presbyterian Medical Center, 168 Street and Broadway from 2 to 6.

SECTION OF ORTHOPEDIC SURGERY—March 20

I. READING OF THE MINUTES.

II. PAPERS OF THE EVENING—a. Fractures of the ankle, Kenneth M. Lewis; b. Some principles in treatment of fractures about the shoulder, Clay Ray Murray; c. 1. Functional method of treating humeral shaft fractures, 2. Ambulatory method of treating femoral shaft fractures, Roger Anderson, Seattle (by invitation).

III. GENERAL DISCUSSION.

IV. EXECUTIVE SESSION—Appointment of Nominating Committee.

SECTION OF OBSTETRICS AND GYNECOLOGY—March 24

I. PRESENTATION OF CASE REPORT AND PATIENT—Sacrococcygeal transrectal repair of high rectovaginal fistula incidental to sacral Mikulicz Vorlagerung for rectosigmoidal carcinoma, John C. A. Gerster; Discussion opened by Raymond R. Squier (by invitation), Royal C. Van Etten, David N. Barrows.

II. PAPERS OF THE EVENING—a. Primary ovarian pregnancy, with report of an interesting case, Mortimer N. Hyams; Discussion opened by Anthony Wollner, Ward J. McNeal; b. The blood oestrin test of Frank and Goldberger, Theodore Neustaedter; Discussion opened by Gertrude Felshin; c. The care and feeding of the newly born, Charles Hendee Smith; Discussion: John Taylor Howell, Jr., Hugh Chaplin.

III. GENERAL DISCUSSION.

COMBINED MEETING OF THE NEW YORK PATHOLOGICAL SOCIETY and the SECTION OF PEDIATRICS—March 26

I. SYMPOSIUM ON SPLENOMEGALY IN CHILDHOOD—a. Pathological aspects, Paul Klemperer; b. Clinical aspects, Rustin McIntosh.

II. DISCUSSION—Margit Freund, David Perla, Maurice N. Richter, Nathan Rosenthal, William P. Thompson.

III. EXECUTIVE SESSION—Section of Pediatrics—Appointment of Nominating Committee

AFFILIATED SOCIETIES

NEW YORK ROENTGEN SOCIETY in affiliation with THE NEW YORK ACADEMY OF MEDICINE

March 16

I. PAPERS OF THE EVENING—a. Etiology of silicosis and its medico-legal considerations, Harrison S. Martland, Newark (by invitation); b. Roentgen findings in silicosis, Raphael Pomeranz, Newark (by invitation).

II. Discussion—J. Burns Amberson, Wm. Cole, L. J. Goldwater.

III. Executive Session.

NEW YORK MEETING of the SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE

March 18

I. Differential bile acid analysis in various pathological conditions, H. Doubilet, R. Colp (Introduced by L. Gross).

II. Anaphylaxis and cerebral allergy in the monkey (*Macacus rhesus*), N. Kopeloff, L. M. Davidoff, L. M. Kopeloff.

III. Effect of extirpation of pituitary gland on arterial blood pressure of dogs with experimental hypertension, I. H. Page, J. E. Sweet.

IV. Some effects of hypophysectomy on the reproductive system and its responses to ovarian hormone in Rhesus monkeys, P. E. Smith, H. H. Tyndale, E. T. Engle.

V. Effect of hypophysectomy on blood sugar of Rhesus monkeys, P. E. Smith, L. Dotti, H. H. Tyndale, E. T. Engle.

VI. Functional auto- and homoplastic thyroid grafts in the rat, T. N. Salmon, A. E. Severinghaus.

VII. Gangrenous and ulcerative lesions of the toes following injections of tobacco in rats, M. Friedlander, S. Silbert, N. Laskey (Introduced by L. Gross).

VIII. Role of pepsin in experimental production of gastric ulcer in rats, M. J. Matzner, C. Windwer, A. E. Sobel, S. H. Polayes (Introduced by B. Kramer).

IX. Multi-plane chest electrocardiography, J. Weinstein (Introduced by M. A. Rothschild).

NOTICES

SECTION OF HISTORICAL AND CULTURAL MEDICINE

As the Section arranged the program of the Stated Meeting of the Academy for March 5, the regular meeting was not held on March 11.

SECTION OF PEDIATRICS

The regular meeting of the Section of Pediatrics was not held on March 12th. Instead, the Section held a combined meeting with the New York Pathological Society on March 26th.

APRIL

STATED MEETINGS

April 2

I. Executive Session—a. Reading of the Minutes; b. Election of Members.

II. Papers of the Evening—A Study of the Diseases Amenable to Splenectomy—a. The advantages of the combined clinic in middle ground disease, Allen O. Whipple; b. Idiopathic thrombocytopenic purpura. A review of 23 cases with the results of splenectomy, Daniel Brown, R. H. E. Elliott, Jr.; c. The role of congestion (portal hypertension) in the Banti syndrome and the response to splenectomy, L. M. Rousselot; d. Hemolytic jaundice—its recognition, treatment and behavior, W. P. Thompson.

THE HARVEY SOCIETY (IN AFFILIATION WITH THE NEW YORK ACADEMY OF MEDICINE)

April 16

The Seventh Harvey Lecture, "Malignant Cells," Warren H. Lewis, Research Associate, Carnegie Institution of Washington, Professor of Physiological Anatomy, Johns Hopkins University.

SECTION MEETINGS

COMBINED MEETING OF SECTION OF SURGERY AND SECTION OF PEDIATRICS—April 3

I. Reading of the Minutes.

II. Presentation of Cases—Two cases of mesenteric lymphadenitis, Henry W. Cave.

III. Papers of the Evening—a. Acute mesenteric lymphadenitis simulating acute appendicitis, Henry W. Cave, Robert Shaw (by invitation); Discussion, Edward W. Peterson, Murray H. Bass, Edward J. Donovan; b. Hirschsprung's disease, Edward W. Peterson; Discussion, Edward J. Donovan, Sidney V. Haas, George D. Scott; c. Anomalies of structure and derangement of function in the gastrointestinal system in children, Charles Gilmore Kerley; Discussion, John Caffey.

IV. Discussion—Murray H. Bass, John Caffey.

V. Executive Session—Nomination of Section Officers and one Member of Advisory Committee.

SECTION OF DERMATOLOGY AND SYPHILOLOGY—April 7

I. Reading of the Minutes.

II. Presentation of Cases—a. New York Hospital & Cornell Medical College; b. Miscellaneous cases.

III. Discussion of Selected Cases.

IV. Executive Session—Nomination of Section Officers and one member of Advisory Committee.

SECTION OF NEUROLOGY AND PSYCHIATRY—April 14

I. Case Presentations—a. Extradural lipoma compressing the spinal cord, Anatole Kolodny (by invitation); Discussion, Herman Schwartz, R. Cohen; b. Cervical cord tumor resembling combined system disease, E. D. Friedman; Discussion, Foster Kennedy, Henry Alsop Riley.

II. Papers of the Evening—a. The torula infection of the central nervous system, S. Philip Goodhart, Charles Davison; Discussion, Henry Alsop Riley, S. W. Gross, Leon H. Cornwall; b. Behavior problems in children of psychotic parents, Lauretta Bender; Discussion, Justice Jacob Panken of the Childrens' Court (by invitation), Florence Powdermaker (by invitation); c. The prepsychotic personality of the anxious, agitated depression, Wm. B. Titley (by invitation); Discussion, Philip R. Lehrman.

III. Executive Session—a. Report of Resolutions Committee; b. Nomination of Section Officers and one member of Advisory Committee.

SECTION OF OTOLARYNGOLOGY—April 15

PROGRAM PRESENTED BY THE STAFF OF OTOLARYNGOLOGY OF THE NEW YORK HOSPITAL

I. Reading of the Minutes.

II. Presentation of Memorial for Edward Bradford Dench by Thomas J. Harris.

III. Presentation of Cases—Illustrating the Papers of the Evening—a. The incidence of sinusitis and nasal polypi in bronchial asthma, Samuel F. Kelley (by invitation); Discussion by John D. Kernan; b. Recurrent lipoma-myxochondroma-fibroma of larynx, Arthur Palmer; c. Demonstration of ear drum models, Gervais W. McAuliffe; d. The effect of intranasal phenol application in hay fever quantitatively studied by intranasal swab tests with pollen extracts, Fernand Vistreich (by invitation); e. Roentgen ray therapy of carcinoma of the nose and throat, Alfred F. Hocker (by invitation); Discussion by Henry H. Forbes, Marvin F. Jones.

IV. Executive Session—Nomination of Section Officers and one member of Advisory Committee.

SECTION OF GENITO-URINARY SURGERY—April 15

I. Reading of the Minutes.

II. Presentation of New Instrument—A new self-lubricating catheterizing forceps, Raymond E. Tyvand, Dayton, Ohio (by invitation).

III. Presentation of Cases—Suprarenal tumors. A report of two cases, Howard S. Jeck, E. Hall Kline, Nyack, N. Y. (by invitation).

IV. Papers of the Evening—a. Precancerous dermatosis of the penis, with the presentation of a case, Archie L. Dean, Jr., Joseph H. Farrow (by invitation); Discussion by Marion B. Sulzberger; b. Pelvic plication in the treatment of hydronephrosis,

Seymour F. Wilhelm, George Blinick (by invitation); Discussion by George Cahill, Oswald Swinney Lowsley, John H. Morrissey.

V. General Discussion—Stanley R. Woodruff, Thomas J. Kerwin.

VI. Executive Session—Nomination of Section Officers and one member of Advisory Committee.

SECTION OF ORTHOPEDIC SURGERY—April 17

I. Reading of the Minutes.

II. Presentation of Cases—a. Arthroplasty of the knee, Samuel A. Jahss (by invitation); b. Arthroplasties of the hip, Halford Hallock; c. One good and one bad arthroplasty of the knee, Joseph E. Milgram (by invitation); d. Arthroplasties of the knee, hip, and elbow, Joseph B. L'Episcopo; e. Cases illustrating one of the papers of the evening, Samuel Kleinberg.

III. Papers of the Evening—a. Arthroplasties of the lower extremity, Samuel Kleinberg; b. Arthroplasties of the elbow, Sumner L. Roberts, Boston (by invitation), Philip D. Wilson.

IV. General Discussion.

V. Executive Session—Nomination of Section Officers and one member of Advisory Committee.

SECTION OF OPHTHALMOLOGY—April 20

Instructional Hour, 7:00-8:00 p.m.—The operative treatment of glaucoma, Webb W. Weeks.

Slit-Lamp Demonstration of Cases—Milton L. Berliner, Girolamo Bonaccalto, Gordon M. Bruce, Wendell L. Hughes.

Regular Program

I. Executive Session—a. Reading of the Minutes; b. Nomination of Section Officers and one member of Advisory Committee.

II. Report of Cases—a. Simple conjunctival suture for cataract section, S. A. Agatston; b. Two tumors of the eye, 1. Amputation neuroma of the long posterior ciliary nerve, 2. Plexiform neuroma of the choroid in a non-buphthalmic eye, L. H. Meeker.

III. Paper of the Evening—Fundus lesions in essential hypertension and arterial and renal diseases, Martin Cohen; Discussion, H. O. Mosenthal, W. W. Herrick, A. J. Bedell, David Wexler.

SECTION OF MEDICINE—April 21

I. Papers of the Evening—Symposium—Recent Advances in Hematology—a. Biological and chemical studies in pernicious anemia, Bernard M. Jacobson, Boston (by invitation) (30 minutes); Discussion, Randolph West (5 minutes), Guy Clark (by invitation); b. The use of placental extract in hemophilia, R. Cannon Eley, Boston (by invitation) (30 minutes); Discussion, William P. Thompson (5 minutes), Francis Wright (by invitation), Carl Smith; c. The use of moccasin venom in bleeding, Samuel M. Peck (30 minutes); Discussion, Nathan Rosenthal (5 minutes), Cornelius P. Rhoads (5 minutes), William Thompson.

II. Nomination of Section Officers and one member of Advisory Committee.

SECTION OF OBSTETRICS AND GYNECOLOGY—April 28

PROGRAM ARRANGED BY THE STAFF OF THE SLOANE HOSPITAL FOR WOMEN

I. Executive Session—a. Nomination of Section Officers and one member of Advisory Committee; b. Other business.

II. Presentation of Case Reports—a. Marsupialization of inoperable ovarian cysts, with case reports, Harbeck Halsted; b. 1. Unusual case of Krukenberg tumor, 2. Spontaneous rupture of heart in new born, John H. Boyd (by invitation).

III. Papers of the Evening—a. Methods for control of morbidity in obstetrical practice, D. Anthony D'Esopo (by invitation); b. Excessive uterine bleeding of functional origin, Raphael Kurzrok, Leo Wilson; c. X-ray studies of the mechanism of labor, William E. Caldwell, Howard C. Moloy (by invitation); d. Pessary treatment of

retroversion and retroflexion of the uterus, William M. Findley (by invitation); e. The mortality following hysterectomy for fibromyomatous tumors, James A. Corscaden.

IV. General Discussion.

AFFILIATED SOCIETIES

NEW YORK MEETING OF SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE—April 15

I. A simple method for determination of ethyl alcohol in blood, J. C. Abels (Introduced by I. Greenwald).

II. Subcutaneous temperatures in localized infections, J. H. Conway (Introduced by P. Reznikoff).

III. Cultivation of poliomyelitis virus *in vitro* in human embryonic nervous tissue, A. B. Sabin, P. K. Olitsky.

IV. Absorption through the nasal mucosa of mice, G. Rake.

V. Hemorrhagic necrotic skin lesions in rabbit produced by *Hemophilus influenzae* and *Hemophilus pertussis*, E. Witebsky, H. Salm.

VI. Prolonged injection of a thyrotropic extract without development of refractoriness, S. C. Werner (Introduced by P. E. Smith).

VII. Quantitative relation between follicle stimulating and luteinizing effects in castrate and menopause urine, U. J. Salmon, R. T. Frank.

VIII. Relation of the cholane nucleus to the female bitterling test for male hormone, I. S. Kleiner, A. I. Weisman, D. I. Mishkind.

NEW YORK ROENTGEN SOCIETY in affiliation with THE NEW YORK ACADEMY OF MEDICINE—April 20

I. Roentgen therapy of vomiting in infants, Theodore West (10 minutes).

II. Papers of the Evening—a. The acute abdomen: Intra-intestinal and extra-intestinal gas, Charles S. B. Cassasa (by invitation); Discussion, Ross Golden, Paul Swenson; b. Mechanical factors in acute respiratory disease of infants with special reference to obstructive emphysema and atelectasis, William Snow; Discussion, Solomon Weintraub (by invitation).

III. Executive Session.

NEW YORK PATHOLOGICAL SOCIETY in affiliation with THE NEW YORK ACADEMY OF MEDICINE—April 23

I. Case Reports (presentation of gross specimens)—a. Dermoid cyst of ovary with squamous cell carcinoma; b. Oophoroma folliculare (Brenner) of ovaries, L. H. Meeker; c. Pedunculated subserous myo-sarcoma of stomach with fatal hemorrhage, A. J. Fried.

II. Papers of the Evening—a. Anaplastic carcinoma of vestibular (Bartholin) gland, S. M. Rabson, L. H. Meeker; b. Congenital defect of heart (cor triloculare biventriculosum), L. H. Meeker, M. M. Maliner (by invitation).

III. Executive Session.

DEATHS OF FELLOWS OF THE ACADEMY

Barany, Robert, M.D., Upsula, Sweden; graduated in medicine from the University of Vienna in 1900; elected an Honorary Fellow of the Academy November 18, 1926; died April 8, 1936.

Dr. Barany received the 1914 Nobel award for medicine for his investigations in physiology.

He was professor of otology, rhinology and laryngology at the University of Upsula, Upsula, Sweden.

BROOKS, HARLOW (HENRY) M.D., 47 West 9 Street, New York City; graduated in medicine from the Department of Medicine and Surgery, University of Michigan 1895; elected a Fellow of the Academy March 3, 1904; died April 13, 1936.

Dr. Brooks was attending physician to Bellevue Hospital and consulting physician to St. Vincent's, City, Montefiore, Joint Disease, Fifth Avenue, French, Polyclinic, Beth Israel, Ossining, Union, St. John's, St. Joseph's, Yonkers, Mt. Vernon, Flushing, Greenwich (Conn.), Hackensack and Norwegian Hospitals.

He was president of the American College of Physicians from 1920-1922 and president of the New York Pathological Society from 1900-1901. He was a Fellow of the American Medical Association; a member of the Association of American Physicians, American Gastro-enterological Society, American Association of Pathologists and Bacteriologists, Harvey Society, American Museum of Natural History, Association for the Advancement of Science, Society for Experimental Biology and Medicine, Alumni Association of City Hospital, Alumni Association of Montefiore Hospital, Society of Alumni of Bellevue Hospital, the County and State Medical Societies, and an Honorary Fellow of the New York Zoological Society.

In 1931, Dr. Brooks received the honorary degree of Master of Science from the University of Michigan. He made many contributions to medical literature. In the World War, Dr. Brooks served, first as chief of the medical service at the Camp Upton Hospital and later in France as chief medical consultant to the First Army and then as senior medical consultant to the Second Army, A. E. F.

His services to the Academy were numerous and important. He was a vice-president of the Academy from 1932-1934 and for ten years he was a member of the Committee on Medical Education, and its Chairman for three years, from 1932-1934.

COLEY, WILLIAM BRADLEY, B.A., M.D., 123 East 53 Street, New York City; received the degree of Bachelor of Arts from Yale University in 1884 and graduated in medicine from Harvard Medical School in 1888; elected a Fellow of the Academy March 3, 1892; died April 16, 1936.

Dr. Coley was surgeon-in-chief emeritus to the Hospital for Ruptured and Crippled; surgeon-in-chief to the Mary McClellan Hospital, Cambridge, N. Y., and consulting surgeon to the Memorial Hospital, the Fifth Avenue Hospital, the Physicians' Hospital (Plattsburg, N. Y.), and the Sharon Hospital (Conn.). He was at one time professor of clinical cancer research at Cornell University Medical School.

He was a Fellow of the American Medical Association, American College of Surgeons, American Surgical Association, Southern Surgical and Gynecological Association, International Surgical Society and a member of the New York Surgical Society, Pathological Society, Radiological Society of North America, American Society for the Control of Cancer, American Association for the Advancement of Science, Harvard Medical Society,

Alumni Association of New York Hospital and the County and State Medical Societies. He was an Honorary Fellow of the Royal College of Surgeons of England and an Honorary Member of the Association of Surgeons of Great Britain and Ireland.

Yale University conferred the degree of Master of Arts on Dr. Coley in 1910 in recognition of his work in surgery. Harvard conferred the same degree on him in 1911.

Dr. Coley was the author of several books and a frequent contributor of articles to medical journals on subjects relating to hernia and cancer.

DUEL, ARTHUR BALDWIN, M.D., 135 East 64 Street, New York City; graduated in medicine from Harvard Medical School in 1894; elected a Fellow of the Academy June 1, 1899; died April 11, 1936.

Dr. Duel had been associated with the Manhattan Eye, Ear and Throat Hospital since 1895 and at the time of his death was Vice-President and Chairman of the Board of Surgeons. He was consulting aural surgeon to the Babies Hospital, Skin and Cancer Hospital, New York Board of Health, and Englewood Hospital; consultant otologist to the Flushing Hospital and Post-Graduate Hospital and consultant otolaryngologist to the North Country Community Hospital, Glen Cove. From 1890-1900 he was connected with the New York Eye and Ear Infirmary and from 1908-1913 he was professor of otology at the New York Polyclinic Medical School.

Dr. Duel was an Honorary Fellow of the Société de Laryngologie des Hôpitaux de Paris, a Fellow of the International Collegium Otolaryngologicum, the American Medical Association, the American College of Surgeons and held a certificate from the American Board of Otolaryngology. He was president at one time of the American Otological Society. He was a member of the permanent committee of the Congrés Internationale d'Oto-Rhino-Laryngologie, the American Laryngological, Rhinological and Otological Society, the New York Otological Society and the New York County and State Societies.

He contributed many articles to textbooks and medical journals on the disease and treatment of the eye, ear, nose and throat.

Dr. Duel was vice-president of the Academy from 1922 to 1924 and served as chairman of the building committee of the Academy from 1923-1933 at the time of the construction of the present building; as a member of the Committee on Library from 1916 to 1921, and as a member of the Board of Trustees from 1924 until his death.

HERRIMAN, FRANK RICHARD, M.D., 30 East 40 Street, New York City; graduated in medicine from the Long Island College Hospital in 1902; elected a Fellow of the Academy April 6, 1921; died April 4, 1936. Dr. Herriman had been at one time assistant professor of otolaryngology at the New York Post-Graduate Medical School and Hospital.

He held the certificate of the American Board of Otolaryngology and was a Fellow of the American Medical Association.

NEMET, GEZA, M.D., 2 East 86th Street, New York City, graduated in medicine from the Royal University of Budapest in 1919; elected a Resident Fellow of the Academy June 7, 1932; died March 1, 1936.

Dr. Nemet was physician and chief cardiologist to the Montefiore Hospital. He was a Fellow of the American Medical Association and a member of the County and State Medical Societies.

ROSENTHAL, MAX, M.D., 36 West 89th Street, New York City; graduated in medicine from the University of Leipzig in 1887; elected a Fellow of the Academy April 5, 1906; died April 3, 1936. Dr. Rosenthal was one of the founders and at the time of his death was president of the board of the Sydenham Hospital. He was consulting gynecologist to the Montefiore Hospital, Beth David Hospital, Bronx Hospital and Lenox Hill Dispensary.

Dr. Rosenthal was a Fellow of the American Medical Association and a member of the New York County and State Medical Societies.

SYDENSTRICKER, EDGAR, M.A., 40 East 10th Street, New York City; received his degree of Master of Arts from Washington and Lee University in 1902; elected an Associate Fellow of the Academy February 21, 1930; died March 19, 1936.

Mr. Sydenstricker was chief statistician of the United States Public Health Service for many years, and organizer and Chief of Service of Epidemiological Intelligence and Public Health Statistics of the League of Nations at Geneva in 1923-24. He was on the staff of President Roosevelt's Committee on Economic Security and at the time of his death was scientific director of the Milbank Memorial Fund. He had been statistical consultant to the New York State Charities Aid Association since 1926 and the United States Public Health Service since 1928.

Mr. Sydenstricker was a lecturer and the author of many books, and contributed frequently to scientific periodicals on subjects of public health, epidemiology, medical economics and social research.

TYSON, HENRY HAWKINS, M.D., 20 East 53 Street, New York City; graduated in medicine from New York University Medical College in 1887; elected a Fellow of the Academy November 6, 1890; died April 18, 1936.

Dr. Tyson was surgeon to the Knapp Memorial Hospital and ophthalmologist to the Sea Breeze Hospital and to the Letchworth Village Hospital. He was clinical instructor of eye diseases in the College of Physicians and Surgeons from 1903-1915.

He was at one time Chairman of the Section of Ophthalmology and a former president of the New York Ophthalmological Society. Dr. Tyson was a Fellow of the American Medical Association, the American College of Surgeons and a member of the Ophthalmological Society, the American Ophthalmological Association and the County and State Medical Societies.

He was the author of many books and articles on diseases of the eye.

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